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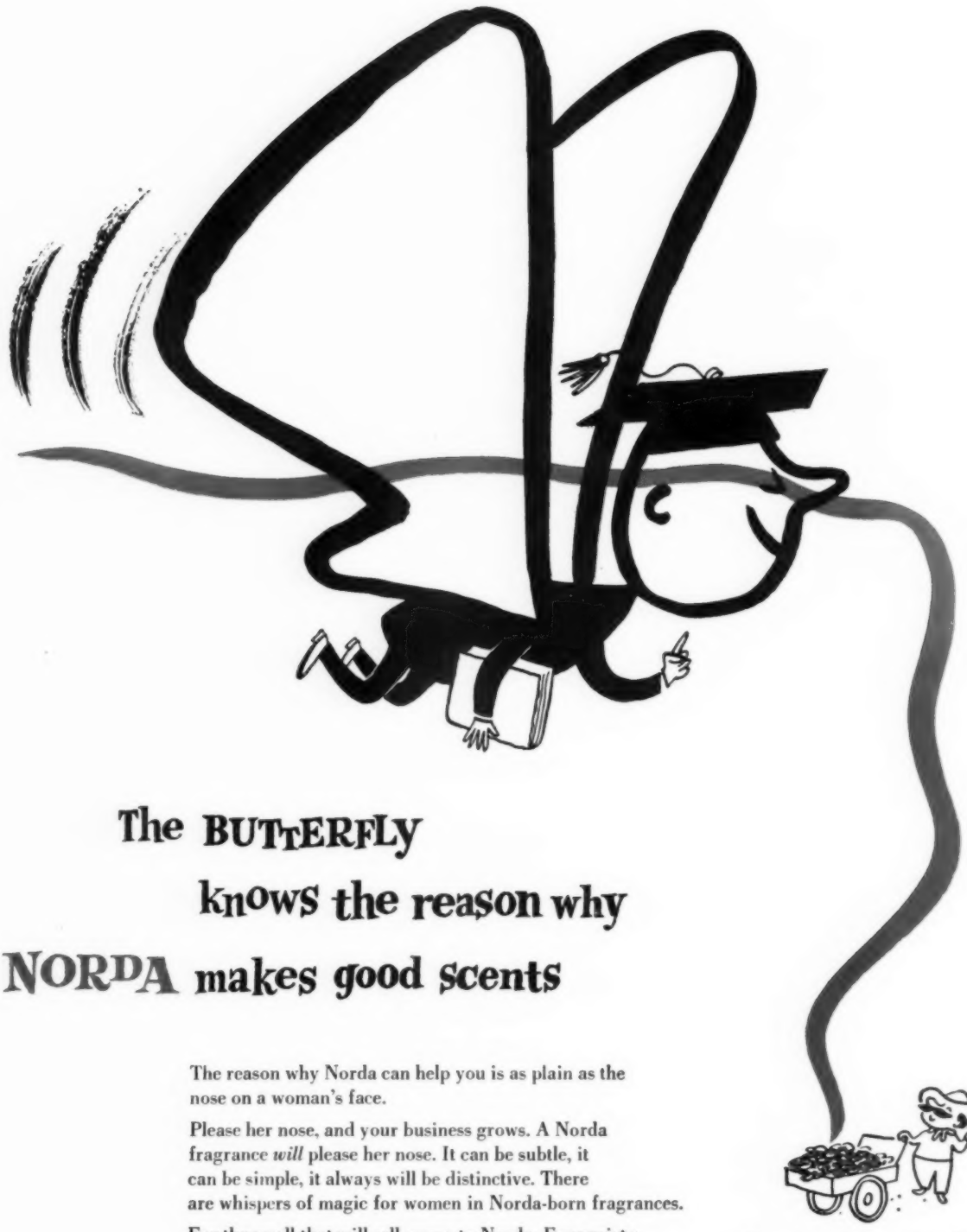
Drug and Cosmetic Industry

OCTOBER 1954



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Drug and Cosmetic Industry

October 1954 Vol. 75 No. 4

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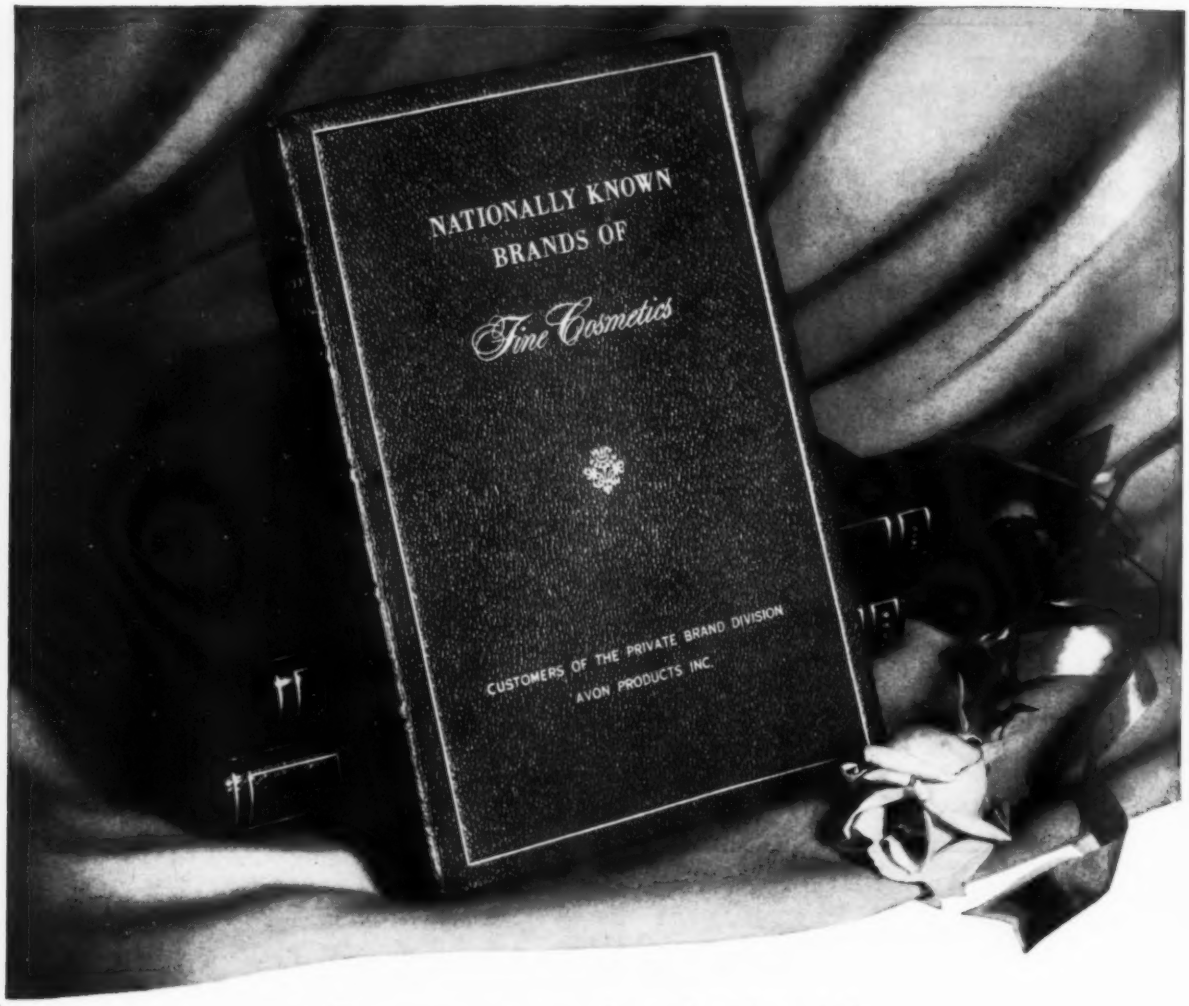

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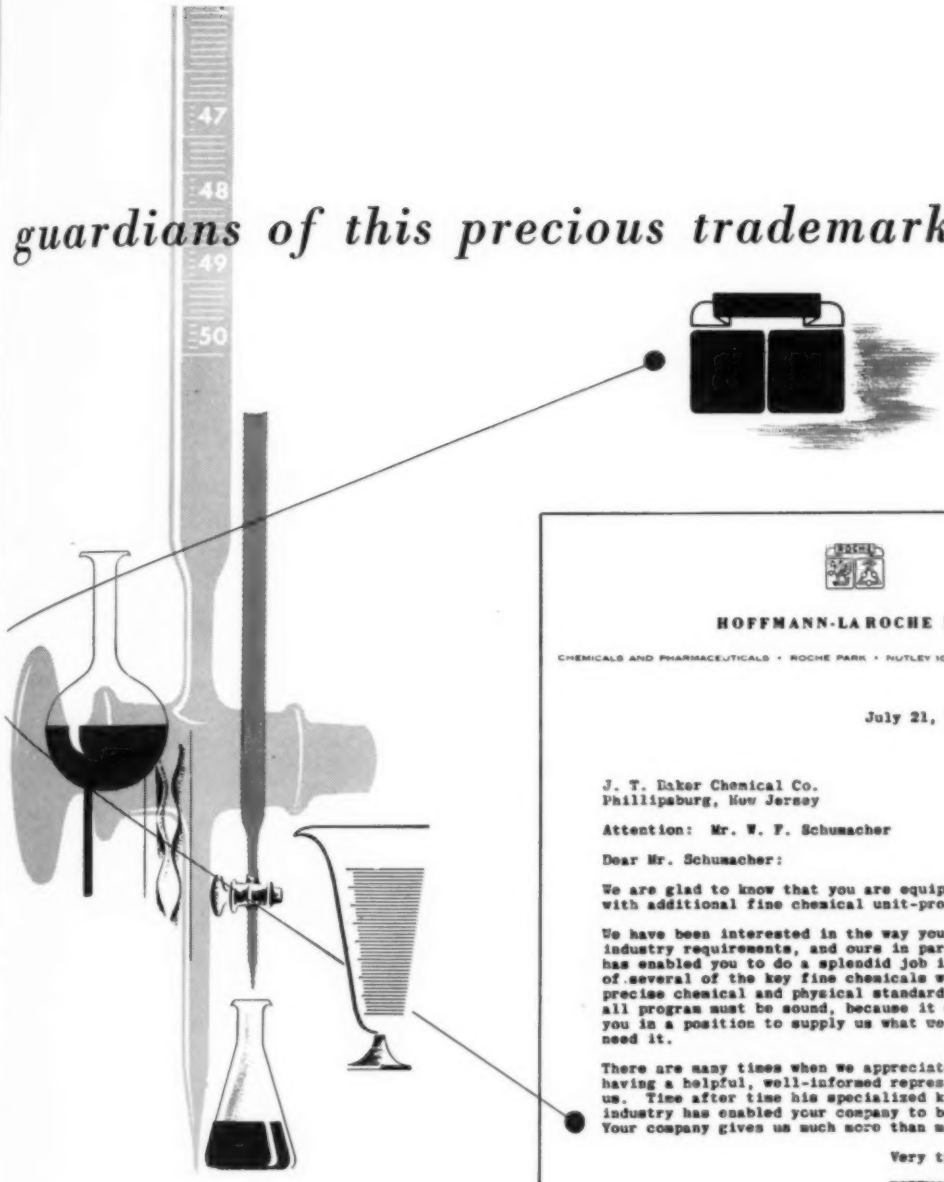

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First, *in vivo*. The imbibing of alcohol raises the level of vitamin A in the blood plasma, provided there is a normal store of it in the liver to draw from. This works so well that it provides a valuable means of finding out if the body is well fixed for vitamin A without the inconvenience of cutting a little piece out of the liver and testing it directly. All that's needed are a few stiff swigs and a sober hematologist. At least some Wisconsin dairy scientists who confined their studies to calves and goats seem to think so.

The *in vitro* picture is of an entirely different character and may be of more interest to your business. Vitamin A esters in alcohol go bad quickly but in a strange way that has nothing to do with oxidation, the usual killer of vitamin A. Instead, the vitamin A esters first split off all their fatty acid, and then you are left with a mixture of anhydro vitamin A, vitamin A ethyl ether, and some decomposition products, but no real vitamin A. Strangely enough, no such decomposition in alcohol takes place if you start out with free vitamin A instead of the more familiar vitamin A esters. There is a slight impediment here to a clear understanding of this situation by those who are not vitamin chemists. That's the fact that "free vitamin A" is known chemically as "vitamin A alcohol." We hope it won't bother you.

The point we'd like to make is that if you have a formulation idea that requires vitamin A to stand up in the presence of alcohol—including glycerine or glycols, which are also alcohols—then vitamin A alcohol may turn the trick. We'd certainly like to work with you in trying it out, or in helping to solve any vitamin A formulation problem, for that matter. You couldn't come to a better or more willing source of vitamin A experience than the makers of Myvax and Myvapack Vitamin A. ***Distillation Products Industries,*** Rochester 3, N. Y. Sales offices: New York and Chicago • W. M. Gillies and Company, Los Angeles and San Francisco • Charles Albert Smith Limited, Montreal and Toronto.

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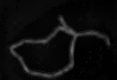

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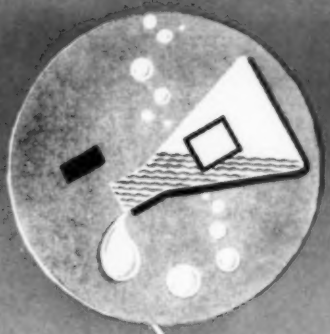

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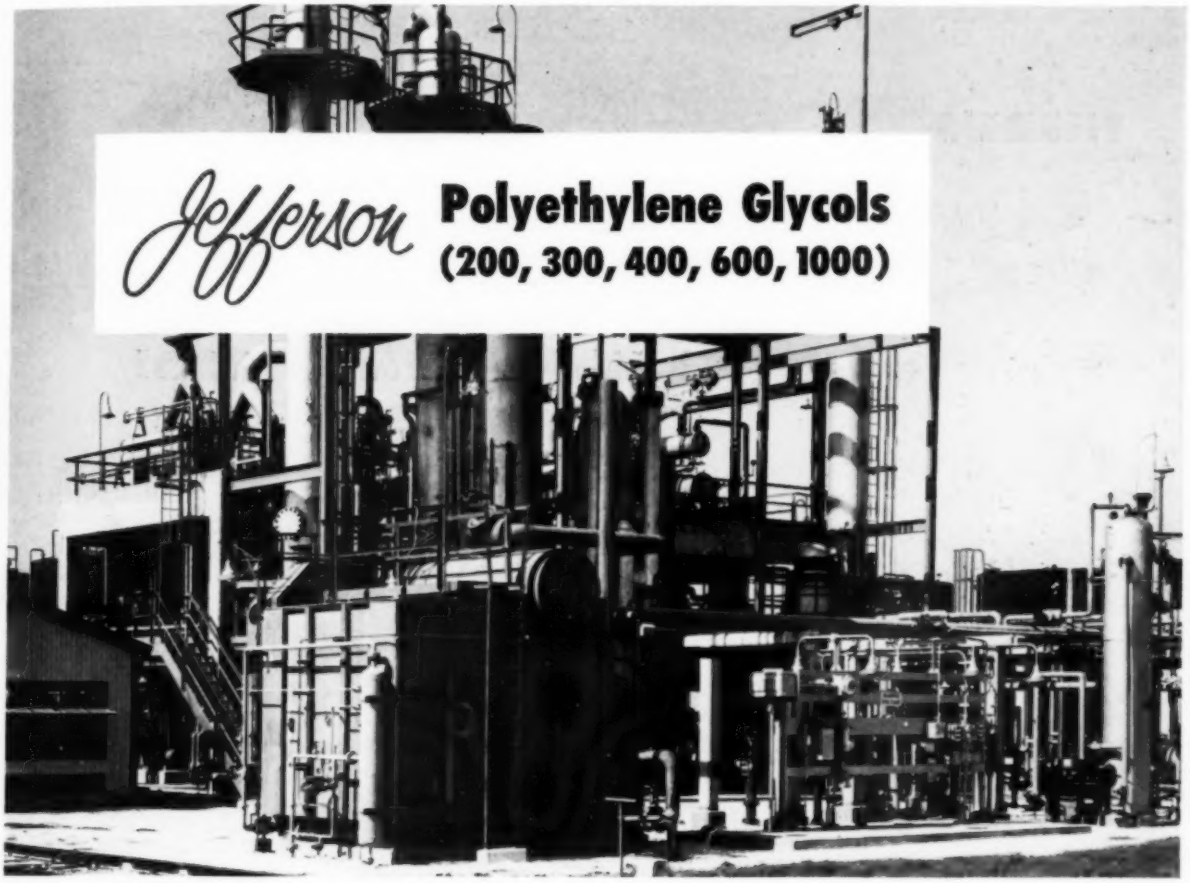

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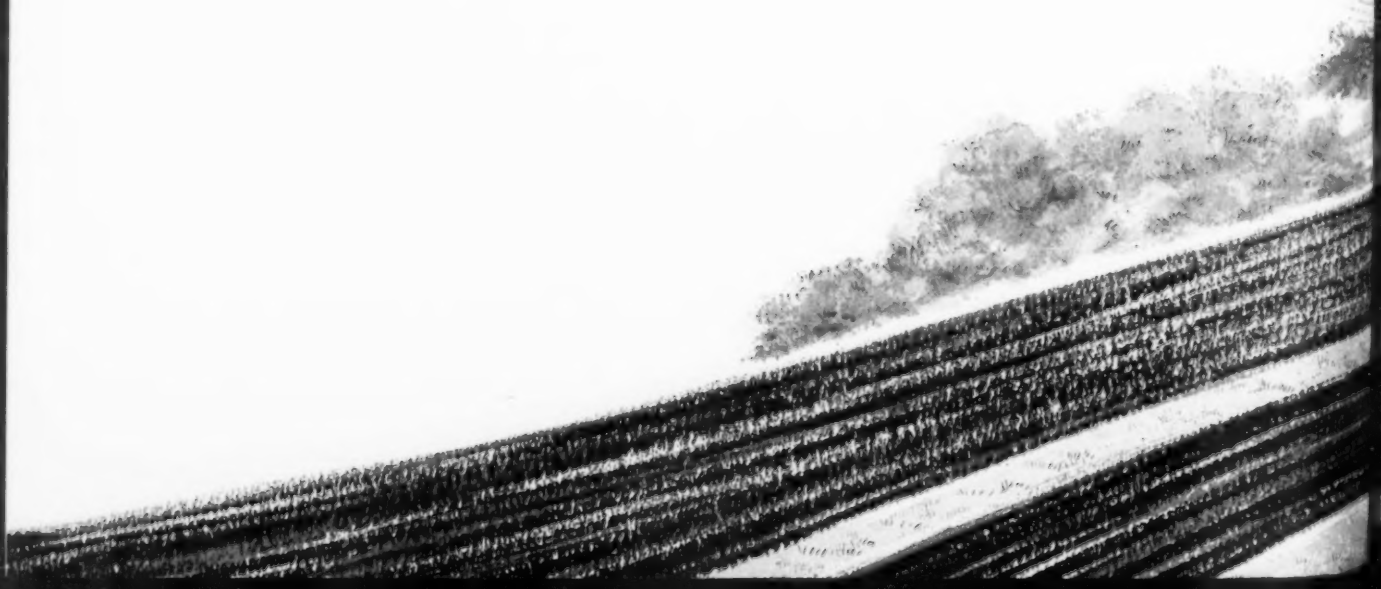

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For technical information and experimental samples, please write Dept. OB-3, B. F. Goodrich Chemical Company, Rose Building, Cleveland 15, Ohio. Cable address: Goodchemco. In Canada: Kitchener, Ontario.

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C-2

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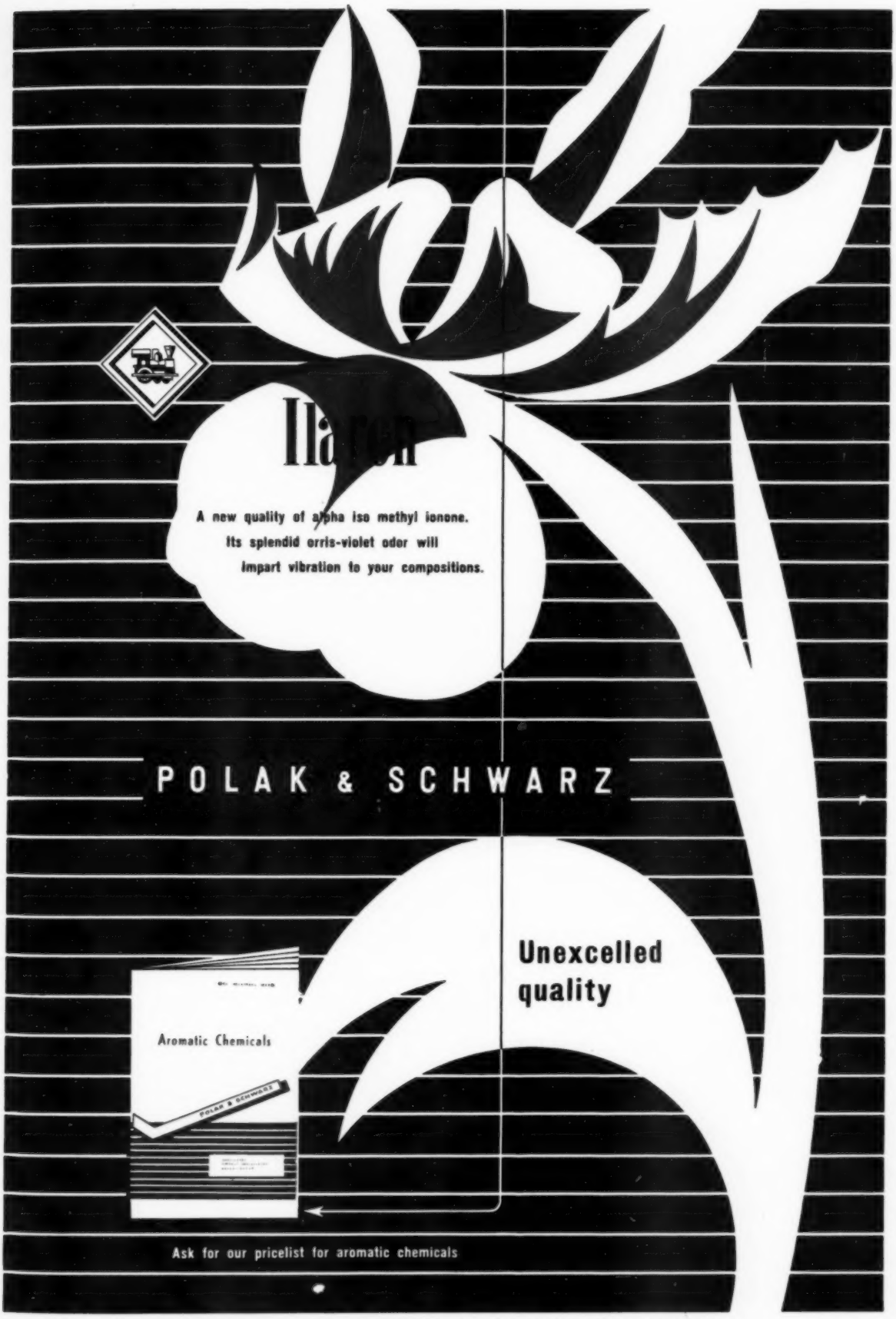
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good ideas have no "office hours"

Here are examples of Pfizer products that cut formulation costs or give you more effective

Economical Vitamin B_{12} Concentrate Oral Grade cuts formulation costs . . . has a high potency (1000 mcg. per gm.). It contains less diluent, so you can use it without enlarging your product. Tablets made with uniformly pink Pfizer Vitamin B_{12} Concentrate Oral grade with its fine-sized particles look more appealing . . . have that characteristically B_{12} color.

Ointments for the treatment of a variety of eye and skin infections are more effective—hence, faster selling—when formulated with Pfizer Neomycin. This antibiotic causes little or no sensitization, and is not absorbed by the skin when administered topically. Administered orally, Neomycin has also been found to be an effective antibiotic for treating many ailments.

That's why your Pfizer sales representative really lives with your problems

Good ideas don't come easily. Especially when you're wrestling with such problems as *how to cut formulation costs... protect label claims... increase product sales appeal... create new products.* This requires more than a little solid thinking and "midnight oil burning." Isn't it a wise step, then, to have the trained, experienced mind of a good salesman working on your problems, too?

Your Pfizer sales representative welcomes this challenge. Why? Because his success is directly related to helping achieve your successes. And to back him up and stimulate his thinking he has the Pfizer Technical Service Department and all the vast experience Pfizer has gained in working with the pharmaceutical industry for over a century. Why not put this thinking and experience to work for you?

preparations with greater sales appeal.

Many manufacturers are improving their hematinic preparations with Pfizer Ferrous Gluconate N.F. The iron in this stable, soluble, non-toxic salt is better tolerated. It does not precipitate proteins and, thus, produces fewer gastrointestinal disturbances. Pfizer Ferrous Gluconate is also more efficiently utilized than iron in other forms – another big sales advantage for your product.

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HLB Method Saves Lab Work in Choosing Surfactants

Up to the early 1930's, cosmetic chemists had few problems in selecting a surfactant. For the great majority of formulas, soap was the most widely used surface active material. In recent years, the number of available surfactants has been enormously multiplied, to better meet the problems of formulating newly-developed emulsion products. Today, the chemist is confronted with the tremendous task of picking from this ever-growing group the compound or blend that will exactly fit his particular formula.

The need for a quantitative method to classify surfactants and to predict their behavior has become more acute with the advent of each new surfactant developed. After extensive experience with surfactant applications, Atlas developed such a method —the HLB System.

What the HLB System is

The HLB System establishes a numerical scale by which surfactants and emulsions can be readily compared. It is developed from the relationship between the behavior of a surfactant and its solubility in water. Chemists have noted for some time that a water-soluble surfactant generally proves most applicable to making an oil-in-water emulsion. Conversely, an oil-soluble surfactant would be the answer to dispersing water into an oil.

Non-ionic surfactants contain in their molecular structure both hydrophilic (water-loving) and lipophilic (oil-loving) groups. When the hydrophilic groups predominate, the surfactant is water-soluble. Large lipophilic groups make the surfactant oil-soluble. In each surfactant, there is a definite balance between these two types of groups.

The HLB number assigned to a surfactant measures the relative strength and size of the hydrophilic and lipophilic groups. On the Atlas HLB scale, the HLB value is a function of the weight percentage of the hydrophilic portion of the molecule.

How HLB is determined

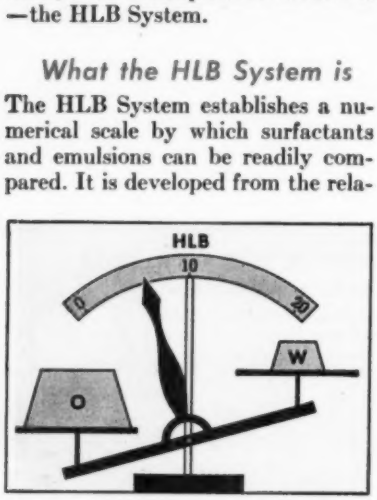
The HLB value for any non-ionic surfactant can be determined experimentally, by a long and laborious procedure. For many basic types of surfactants, however, HLB can be calculated from analytical data by means of empirical formulas developed by Atlas.

If the surfactant is a polyhydric alcohol fatty acid ester, for example, HLB can be calculated from the saponification number of the ester and the acid number of the acid. Where ethylene oxide is the hydrophilic portion, HLB calculation is based on the weight percentage of oxyethylene.

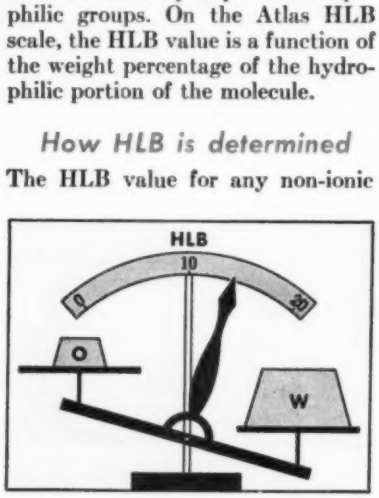
Formulas of this nature give close agreement with experimental data for most non-ionics. In the case of ionic surfactants, calculated HLB values do not follow a weight percentage basis, and the experimental method must be used.

How to use the HLB System

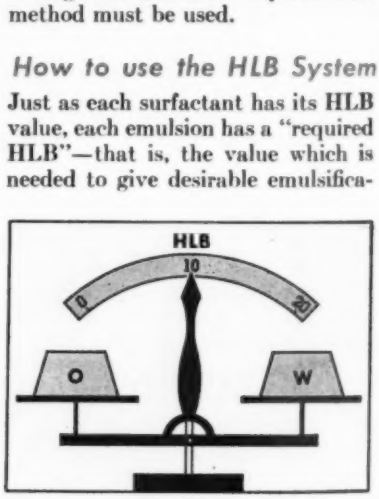
Just as each surfactant has its HLB value, each emulsion has a "required HLB"—that is, the value which is needed to give desirable emulsifica-



When oil-loving groups in surfactant are predominant, HLB is low . . . for producing water-in-oil emulsions.



When water-loving groups predominate, the surfactant has high HLB and is used for oil-in-water emulsions.



When oil-loving and water-loving groups are fairly well balanced, HLB is intermediate (around 10).

tion. "Required HLB" values have been determined for a number of commonly used emulsion ingredients. Some typical values are listed in the table.

HLB values are additive. To obtain the "required HLB" of an emulsion, the HLB of each oil phase constituent is multiplied by its weight percentage in the oil phase. Total HLB is obtained by adding the numbers thus calculated.

Knowing the HLB required for the given emulsion, you can then make an initial selection of a surfactant or blend that will provide this HLB value. HLB is additive for surfactant blends, too. By multiplying the HLB of each surfactant by its weight percentage in the blend, the contribution of each to the total surfactant is obtained. The sum of these values represents the HLB of the combination of surfactants.

"REQUIRED HLB" Values

	W/O Emul.	O/W	Solubilizing (O/W)
Acid, stearic	—	17	—
Alcohol, cetyl	—	13	—
Lanolin, anhydrous	8	15	—
Oil			
Cottonseed	—	7.5	—
Essential	—	—	16.5
Mineral, heavy	4	10.5	—
Mineral, light	4	10-12	15.5
Vitamin (with fats or oils)	—	—	15
Vitamin (fat free)	—	—	16.5
Petrolatum	4	10.5	—
Vitamins			
Esters	—	—	14
Wax			
Beeswax	5	10-16	—
Microcrystalline	—	9.5	—
Paraffin (household)	4	9	—

Chemical identity is important

In addition to having the correct HLB value, a surfactant must also have the proper chemical type for its intended use. This factor is determined empirically at present. Certain chemical types of surfactants are known to work most effectively in definite classes of emulsion applications.

Knowing the required HLB, it is generally advisable to try a variety of surfactants of different chemical types at the optimum HLB. By narrowing the choice to a given HLB range, this system focuses attention on a relatively small number of surfactants out of the thousands available.

A detailed procedure for using the HLB system, and specific recommendations for numerous formulas, are available from Atlas in a booklet titled "A Guide to Cosmetic and Pharmaceutical Formulations." A copy will be sent to emulsion technologists who request it in writing on their company letterhead.

Atlas HLB Selector helps the emulsion formulator by providing a ready reference to recommendations on Atlas surfactants and HLB values for 96 typical emulsion formulas. We'll be glad to send a Selector with full directions to anyone concerned with the preparation of emulsions.

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ANDREAS VESALIUS (1514–1564). Noted Belgian anatomist who was among the first to dissect the human body to study anatomy. His findings were of great value in the advancement of treating disease. Illustration shows him in his room about to begin work on a cadaver.

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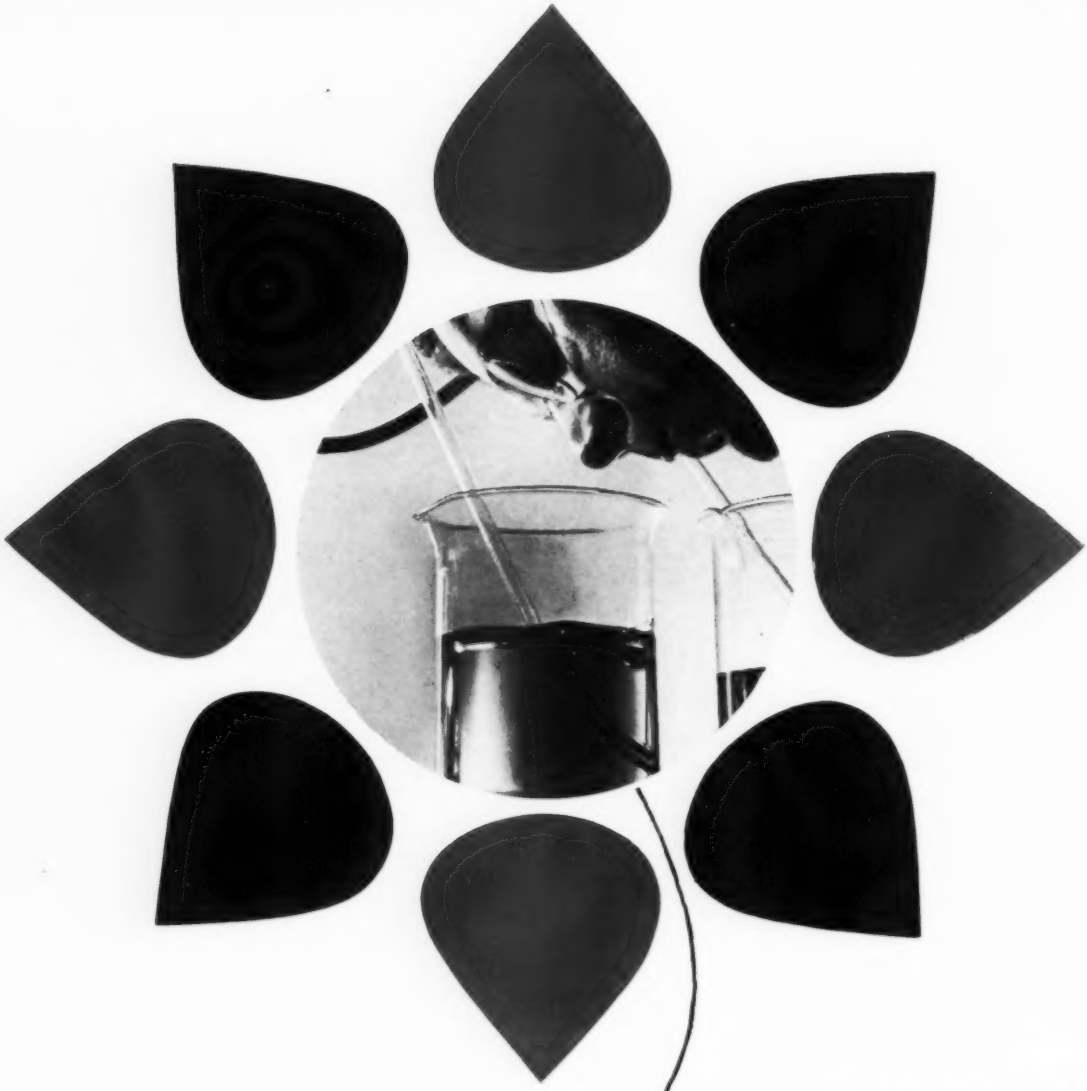

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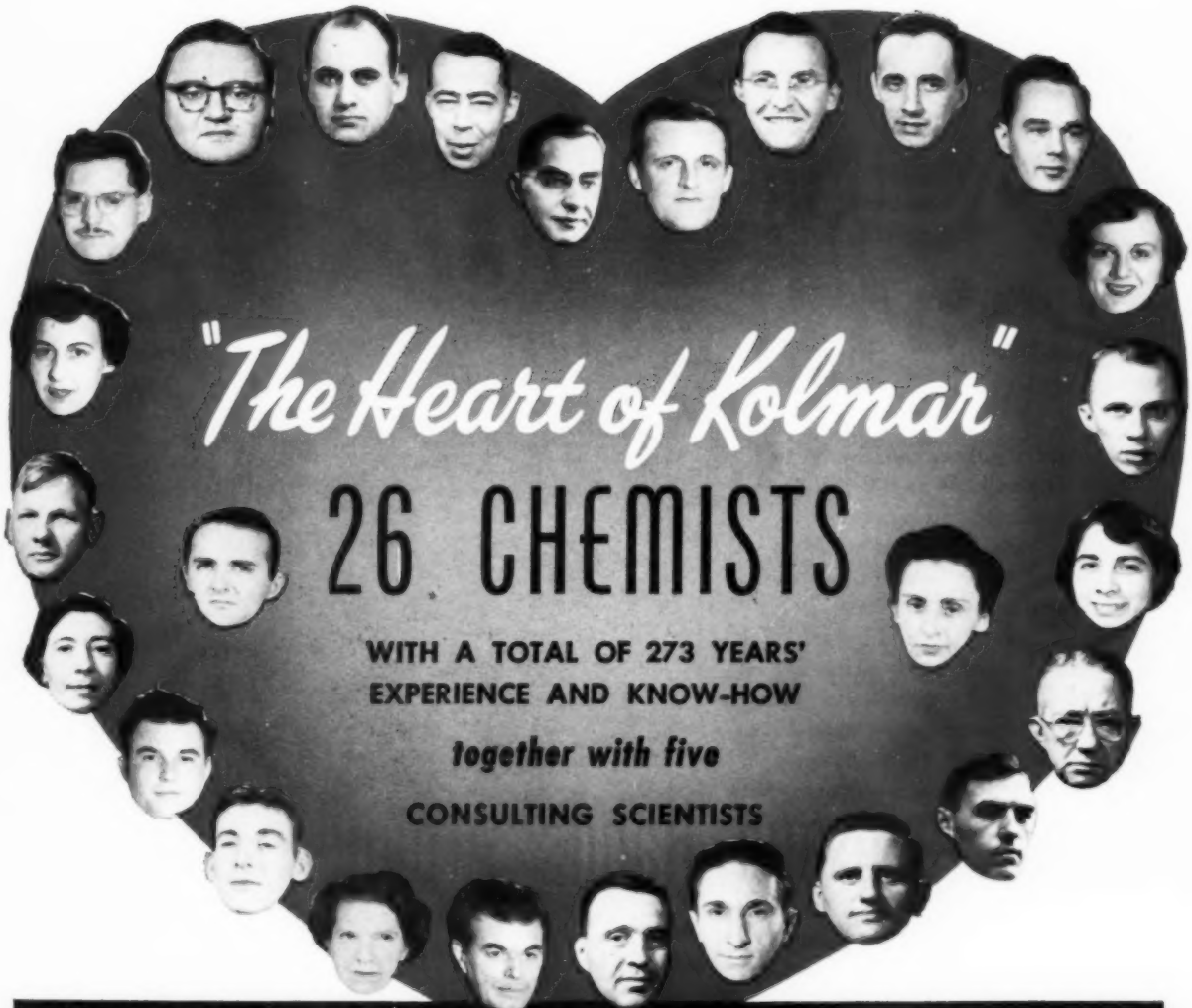
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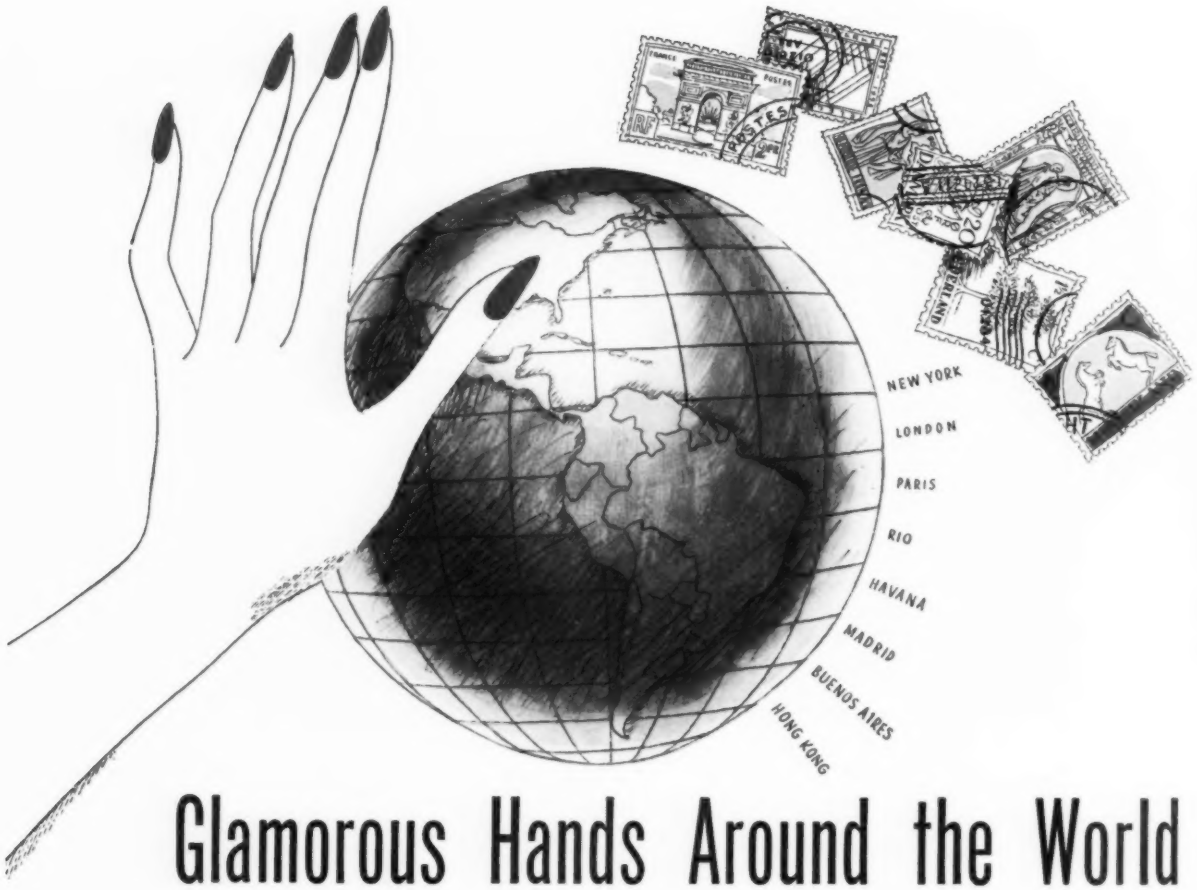

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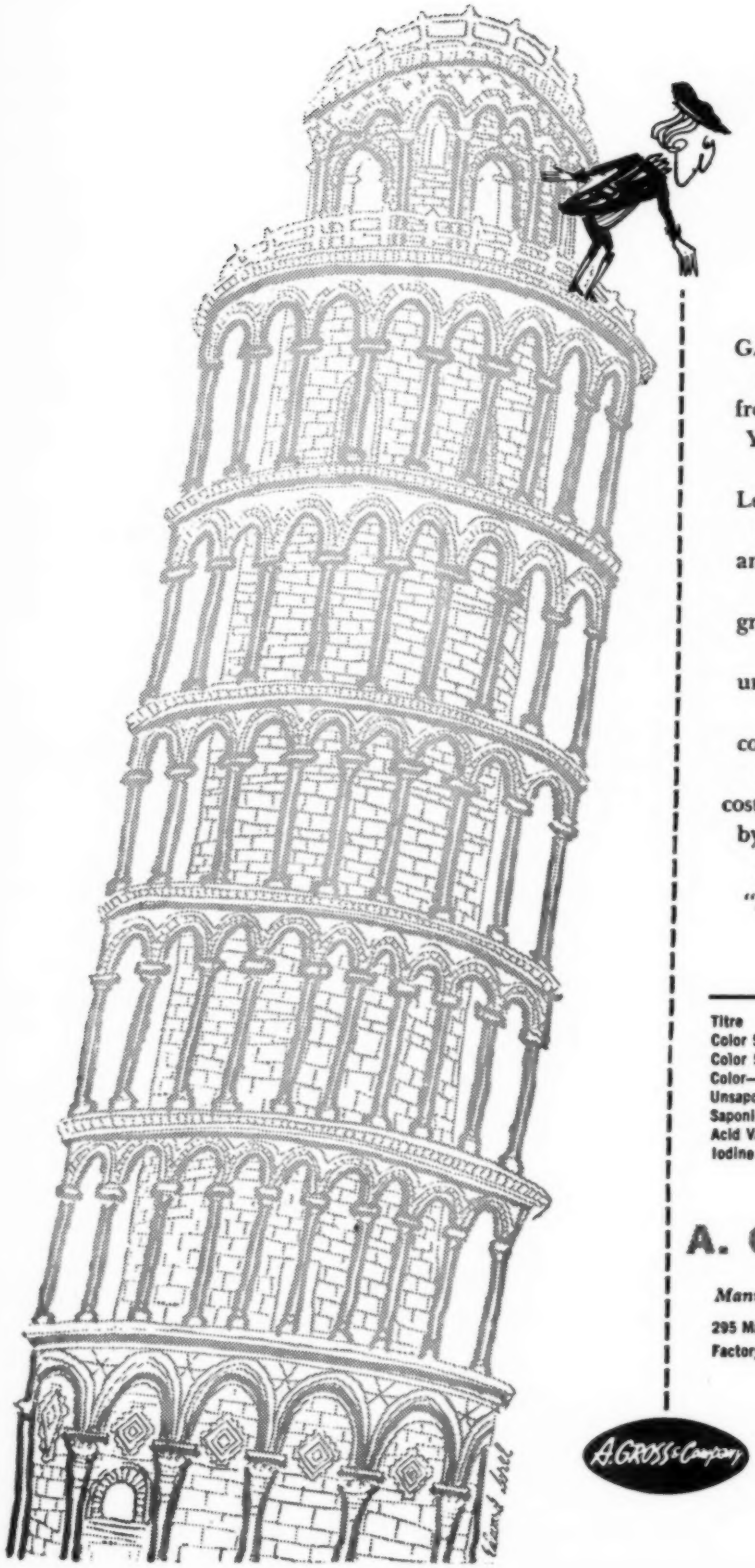

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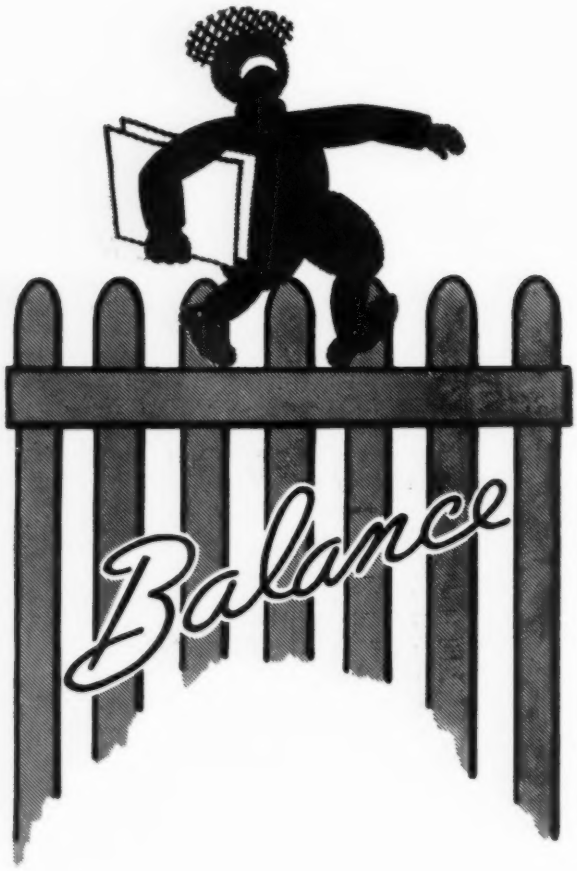

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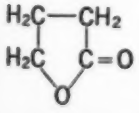
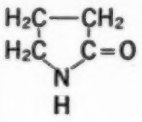
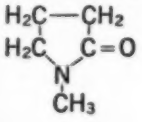
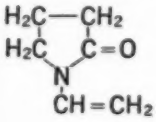
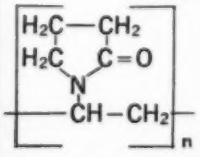
BUTYRO-LACTONE 	Powerful organic solvent for polyacrylonitrile, cellulose acetate, polystyrene, etc. Selective solvent for acetylene in natural gas. Chemical intermediate for aliphatic and cyclic compounds.

2-PYRROLIDONE 	Polymerizes to high molecular weight, linear, nylon-type, polyamide condensation product. Gives γ-aminobutyric acid and derivatives, also N-acyl lactams.
N-METHYL-2-PYRROLIDONE 	Powerful organic solvent for acrylonitrile polymers and copolymers, cellulose triacetate, etc. Selective solvent for acetylene in natural gas. Spinning agent for polyvinyl chloride solution.
N-VINYL-2-PYRROLIDONE 	Will copolymerize with almost all vinyl monomers. Permits modification of many properties in existing homopolymers. Gives control of hydrophobic and hydrophilic properties of products.
POLYVINYL-PYRROLIDONE (PVP) 	Binder, stabilizer, detoxifier, protective colloid, thickener, film former. Physiologically compatible. Wide solubility range. For use in pharmaceuticals, cosmetics, foods, detergents, dye stripping, synthetic fiber additive, size component, lithography, agricultural chemicals, etc.

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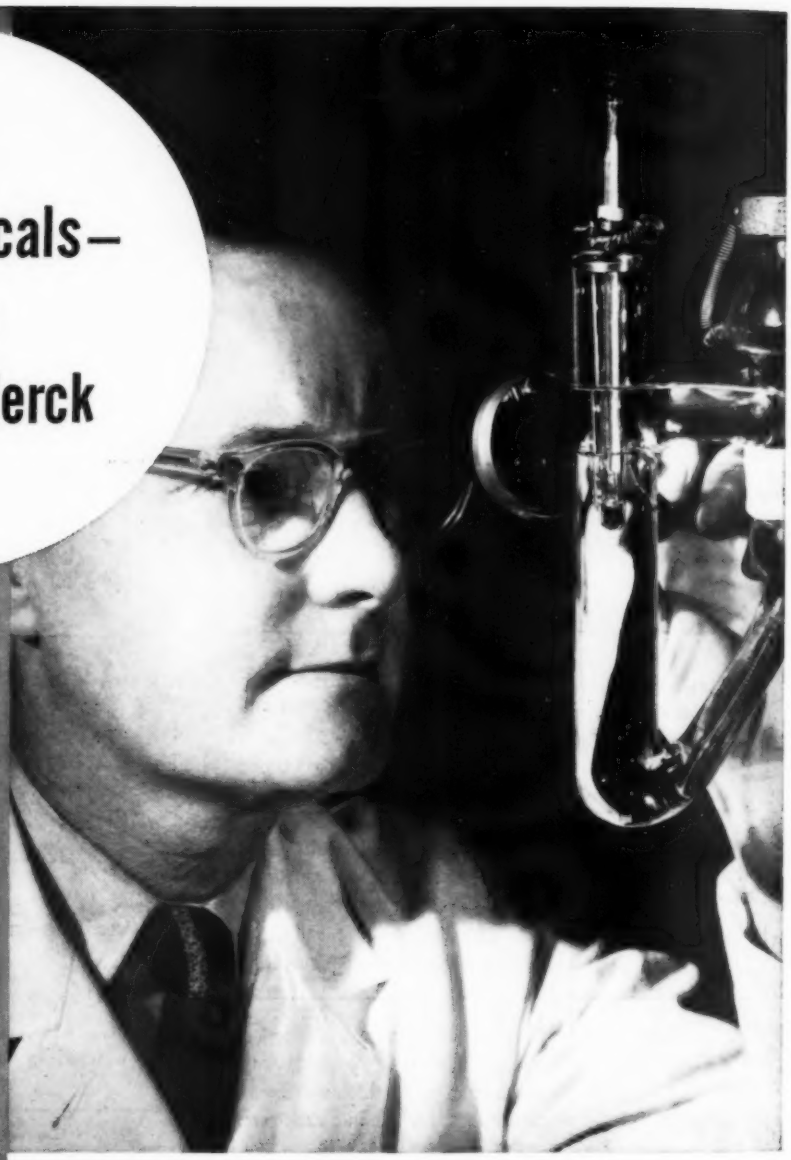

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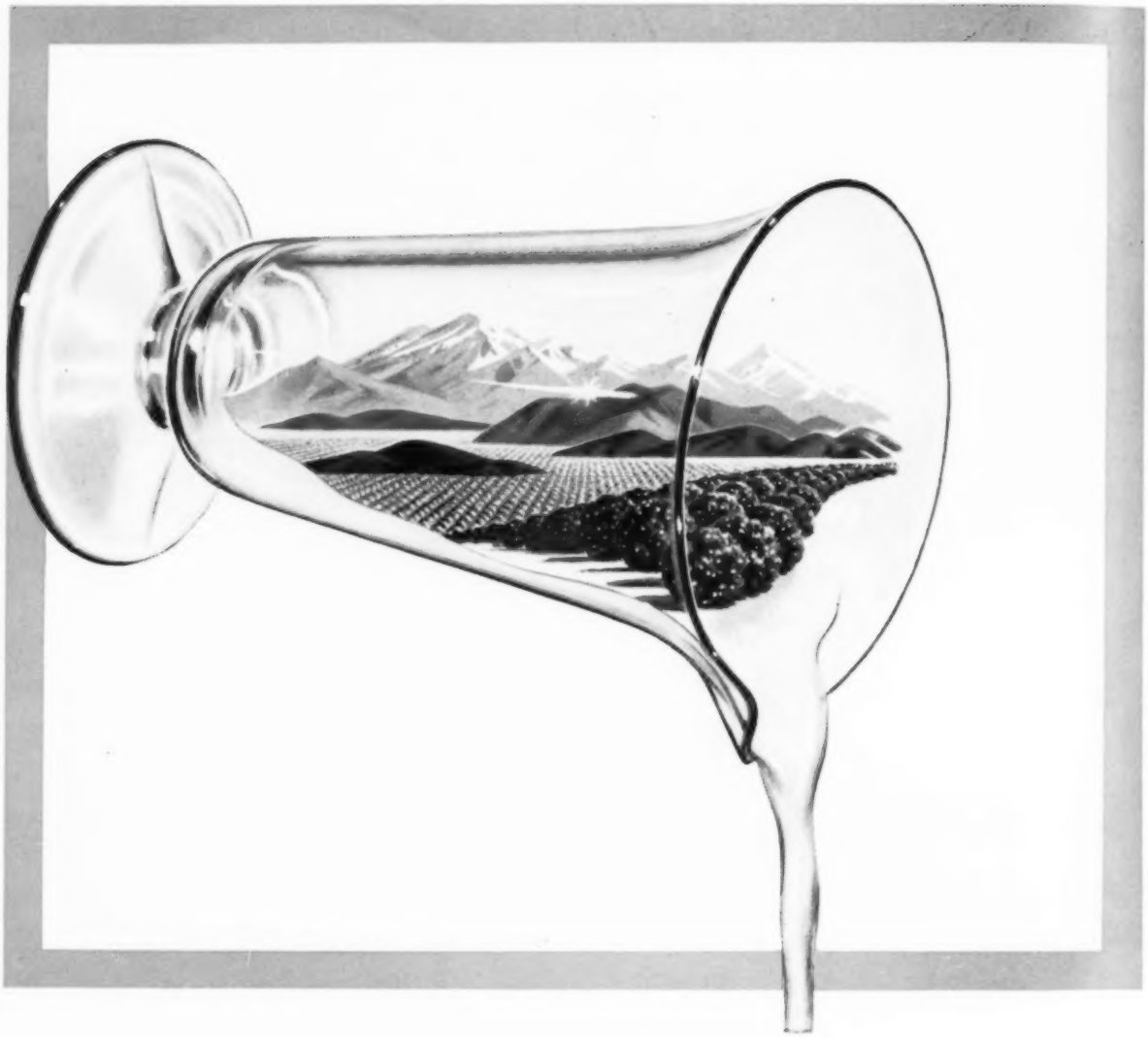

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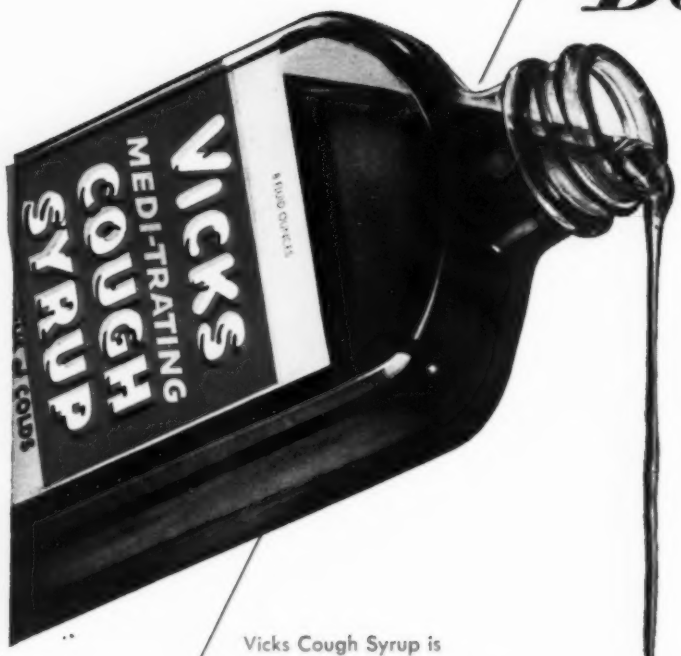


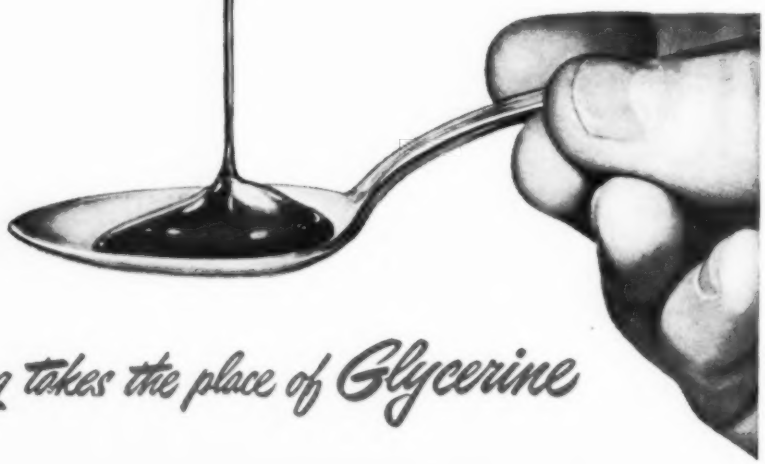
Vicks Cough Syrup is a staple in medicine cabinets all over the world. Its popularity is due in part to the U.S.P. Glycerine contained in the basic formula. Besides making Vicks a more palatable liquid which can be tolerated by children of all ages, Glycerine provides the cough syrup with demulcent and expectorant qualities.

Glycerine is an ideal ingredient for many internal medicines. One important reason is the fact that U.S.P. Chemically Pure Glycerine is non-toxic. It is accepted by medical associations and government agencies as safe for human consumption.

Several other major properties of Glycerine are also important in such uses. In cough syrup for example, it acts as a demulcent, expectorant, dispersing or suspending agent, and sweetener, and adds body to the preparation.

Glycerine is also an important ingredient in many confections, flavoring agents, and other food products.

To get the complete story on why there's no single substitute that combines all of Glycerine's physical and chemical properties, write for your free copies of "Why Glycerine for Foods?" and "Why Glycerine for Drugs and Cosmetics?" Address Glycerine Producers' Association, 295 Madison Avenue, New York 17, New York.



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"An Institute for Veterinary Research that will investigate diseases of pets ranging from the dermatological to the psychological has been announced by the Speyer Hospital for Animals."— New York Times

Keeping Posted

Gamma Globulin Restrictions Removed

The restrictions imposed upon supplies of Gamma Globulin since February, 1953, when it was allocated by the Office of Defense Mobilization under the National Foundation for Infantile Paralysis program, have been lifted. This means that the manufacturers of this product are free to release the product through the usual channels of distribution for the filling of doctors' prescriptions.

Gamma globulin was used as preventive against measles ten or more years ago. A child exposed to measles could be made immune to attack by an injection of gamma globulin. However, this does not prevent the child from getting measles at a later date.

Gamma globulin is described as a grab bag of temporary immunity. It is that part of the human blood which prevents an individual from catching some infectious diseases twice. It carries antibodies developed to combat a disease during illness. Even a light case of infectious hepatitis will produce antibodies. Most adults have antibodies against polio and measles in the gamma globulin of their blood because they have had light cases of these diseases, some perhaps without knowing it. When the gamma globulin from a thousand or more different individuals is pooled together, the pool is certain to contain antibodies against polio, measles, and infectious hepatitis.

Collection and distribution of gamma globulin is an organized way for the immune to lend their immunity to individuals who have no antibodies of their own. As long as the borrowed antibodies remain in the blood, they will prevent or reduce the severity of an attack of the disease against which they were originally manufactured. But after five to eight weeks, the borrowed antibodies pass out of the blood. The main use of gamma globulin then, is to safeguard against an epidemic or a threatened exposure in the immediate future.

Another TV Award to SKF

A special citation for outstanding contribution to medical education was presented last month to Smith, Kline & French Laboratories by the XVII International Congress of Ophthalmology at the Waldorf Astoria Hotel, New York, in appreciation of the "spectacular advance in methods" which it has brought to postgraduate medical teaching through the medium of television.

Prescription Pharmacy Profits

The 1953 study of operating costs of prescription pharmacies, conducted by the American College of Apothecaries, revealed an 8.4 per cent rise of operating costs compared with 1952, thus producing a lower net profit. The average operating expense for all stores studied was 39.7 per cent. Stores deriving more than half their sales from prescriptions had expenses of 40.4 per cent, indicating that average costs increase as the proportion of prescription volume increases.

While the average gross margin for all stores was 44.6 per cent, gross margins increased with a higher portion of sales coming from prescriptions for the gross margin for stores doing more than 50 per cent of total volume in prescriptions was 46.8 per cent.

Although margins increase with added prescription volume, costs increase at a greater proportion revealing that in stores doing under 50 per cent in prescription volume the new profit was 7.1 per cent, while those doing over 50 per cent, the net profit was 6.4 per cent. Since reported sales included approximately 10 per cent of sales to physicians, as well as other sales at a lower margin, it is concluded that gross margins on prescription merchandise must exceed 50 per cent of sales in order to allow for operating costs and a fair margin of profit.

Squibb Offers Antibiotics

E. R. Squibb & Sons is now marketing tetracycline hydrochloride under the trade name, Steclin. The material is said to be supplied to Squibb by Bristol Laboratories. In addition, Squibb is also marketing what is described as the first antifungal antibiotic. This is nystatin, which is sold under the Squibb trade name, Mycostatin.

Squibb explains that an ever-present element in the oral administration of antibiotics, particularly the

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broad spectrum preparations, is the change that may be instigated in the intestinal flora. Frequently, there is a strong overgrowth of Candida albicans (Monilia); the extent of this overgrowth may become greater during prolonged treatment with antibiotics. Symptoms of moniliasis are always a possibility, and in extreme cases generalized moniliasis is the end result.

Tetracycline Patent Status

Chas. Pfizer has revealed the facts concerning present status of the tetracycline patent situation. It appears that Pfizer, in a series of reports in the Journal of the American Chemical Society starting in 1951, gave the results of an intensive investigation of the chemical structures of Terramycin and Aureomycin. The structures of Terramycin and Aureomycin were first published by Pfizer scientists with Professor R. R. Woodward, of Harvard University, in the July 20, 1952 and October 5, 1952 issues of the Journal of the A.C.S., respectively.

Pfizer points out that the discovery of tetracycline, whose structure has a great deal in common with those of Terramycin and Aureomycin, was a key step in this investigation. It was disclosed in the October 5, 1952 publication and, in addition, this article proposed for the first time the name tetracycline from which are derived the related names, oxytetracycline (Terramycin), and chlorotetracycline (Aureomycin).

In the September 20, 1953 issue of the J.A.C.S., both Pfizer and Lederle scientists published detailed papers describing a hydrogenation process for producing tetracycline from Aureomycin. On October 1, 1953, Heyden Chemical Corporation announced that it too, had developed a broad-spectrum antibiotic, believed to be tetracycline, which it had produced by a fermentation process. The Pfizer, Lederle, and Heyden research groups each delivered papers on tetracycline at a symposium on antibiotics held in Washington, D.C. on October 28 to 30, 1953. On November 5, 1953, Bristol Laboratories announced that it, too, had developed a fermentation process for the production of the new antibiotic.

The sequence in the filing of patent applications by these companies was substantially the same. Pfizer filed its first application claiming tetracycline, its salts, and the hydrogenation process in October 1952. Lederle's application, with similar claims, followed in March 1953. Heyden's application claiming tetracycline, its salts, and a fermentation process, was filed in late September 1953. Bristol filed with claims similar to these of Heyden in late October 1953.

The filing of these conflicting claims gave rise to interference proceedings in the Patent Office. The first interference was declared at the end of December 1953 involving a claim to the product, tetracycline, by Pfizer and Lederle. The Heyden application had been acquired shortly before by Lederle when it purchased Heyden's entire antibiotic facilities. Lederle chose to contest the interference with its own application rather than with Heyden's. The Bristol application was excluded from the interference on the ground that it had been filed too late to make the claim in issue (more than a year after the Pfizer October 5, 1952 publication in the J.A.C.S.)

The first interference between Pfizer and Lederle was settled by an agreement under which the parties would compare dates as to priority of invention and concede the priority accordingly. The winning party was to license the other under any patent it obtained for tetracycline in all its customary forms. Since the hydrogenation process for producing tetracycline, which was also involved in the interference, uses Aureomycin as a starting material, Pfizer obtained as part of the settlement agreement a license under Lederle's patent covering Aureomycin to produce Aureomycin for conversion to tetracycline. After comparison of the respective invention dates as provided in the settlement agreement, Lederle conceded priority to Pfizer thereby terminating the first interference early in February 1954.

After the Patent Office rejected all of Bristol's tetracycline product claims on the basis of Pfizer's October 5, 1952 publication, Bristol filed a second application in January 1954 specifically directed to various salts of tetracycline including the hydrochloride. The Patent Office then declared a second interference on the conflicting claims of tetracycline hydrochloride by Pfizer, Bristol, and Lederle (Heyden). It is this interference which is still pending.

One of the key issues is whether Pfizer's October 5, 1952 publication disclosing tetracycline also deprives Bristol of the right to claim the hydrochloride salt. If the Patent Office decides that Bristol does not have this right, Pfizer should receive promptly a broad patent covering tetracycline in the form of its base and its salts including the hydrochloride. Lederle, already having contested priority in the first instance and having conceded to Pfizer, will presumably be barred from again contesting priority on the basis of its Heyden case.

In the event of any other decision the interference will proceed to the taking of testimony to establish the respective invention dates. Such procedures take many months to complete.

Late last month, American Cyanamid Company—of which Lederle Laboratories is a division—filed a suit against Bristol Laboratories in the U. S. District Court for the Northern District of New York, claiming infringement by Bristol of Cyanamid's patent covering chlortetracycline (Aureomycin). The suit charges that Bristol is making and selling an antibiotic composition (tetracycline hydrochloride under the trade name Polycycline) which contains material covered by Cyanamid's patent, and that in making its product Bristol uses processes and methods covered by Cyanamid's patent.

In commenting on this suit, Frederic N. Schwartz, president of Bristol Laboratories, emphasized that the patent involved in the suit was issued in 1949 and relates solely to Aureomycin (chlortetracycline), and flatly denied that Bristol's production of tetracycline involves any infringement of this patent. He added: "This appears to be simply one more incident in the prolonged dispute between Bristol, American Cyanamid, and Pfizer over the inventorship of tetracycline, and can probably be fairly characterized as a fishing expedition. Under no circumstances will the pendency of this suit affect Bristol's production and sale of tetracycline, nor the ultimate ownership of the tetracycline patent which is yet to issue."

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New Lederle Antibiotic

Lederle scientists have discovered a new antibiotic named Puromycin which they think has major potential importance as a building block for better and more effective drugs for the future. At the recent American Chemical Society meeting, the Lederle researchers said they believed that in cases in which Puromycin itself does not prove helpful, it will be possible to make the drug synthetically, altering its molecule to produce "tailor-made" derivatives for fighting disease germs.

The Lederle scientists are excited over the fact that Puromycin acts against tiny, one-celled "animals" called trypanosomes which cause African sleeping sickness. The drug is the first antibiotic, they say, to show activity against this kind of disease organism. It has also knocked out breast cancer in mice. Although the drug apparently does not work on human cancer, the scientists report it may well aid research to produce a substance that does.

The Lederle doctors believe that the drug works by blocking the metabolism of some types of living cells. Using it, they think they may be able to produce drugs counterfeit the chemicals which viruses, bacteria, and cancer cells live on. The materials being only counterfeits, however, instead of helping the disease organisms, would starve or kill them.

The Cost of Drugs

Newall Stewart, executive vice-president of the National Pharmaceutical Council, and president of the American Pharmaceutical Association, told the annual meeting of the Federal Wholesale Druggists Association last month that "uppermost in the minds of most of our pharmacists today is the complaint from the public about the cost of medications. You and I know we do not have to justify these charges, but do we let the public know? Do we accept the figure of $15 billion as the total cost of illness, with our drugs and drug sundries comprising only 10 per cent of this overall total?

"The $15 billion cost of illness represents only about five per cent of our national income, and the ten per cent spent for all forms of drugs represents one-half of one per cent of that income. When compared with expenditures made for many of the luxuries we enjoy, the amount becomes insignificant. We are certainly called upon to inform, not only the public but also the members of our associated health professions, that they are purchasing health and even life at a phenomenally low figure. Pharmacists are making available types of medication which have long since passed the old 'shotgun' type of prescription. These old mixtures, with their hit or miss reactions, have been replaced by today's especially tailored medications—medications which have progressively decreased the length of illness with its attendant costs.

"The widespread public position that drugs are excessively expensive due to collusion between pharmacists and drug manufacturers, is economically irrational and politically dangerous. Yet, millions of persons who are involved in buying for less and selling for more, or manufacturing at one price and selling at a profit, hold that opinion. To tell them that they are illogical is not especially persuasive. Perhaps this is because the public has a tenable position in relation to the cost of drugs. Not tenable in fact, but tenable in terms of the public's psychological reaction to the purchase of drugs."

Sulfa Drug Production

Production of sulfa drugs in the United States in 1953 totaled 4,672,000 pounds, according to figures of the U. S. Tariff Commission released last month. This makes these drugs the leading anti-infective agents by a wide margin, according to a leading manufacturer.

Only one drug was produced in greater quantity than the sulfa drugs and that was aspirin of which 13,713,000 pounds were produced in 1953. Assuming that all this aspirin was made up in five-grain tablets and taken two at a time for relief of headache or other pain, the number of two-tablet doses would be close to one billion.

Synthetic Citral, Linalool, Etc.

Having been dependent upon lemongrass oil as a source of citral from which to make beta-ionone as a raw material for the manufacture of synthetic vitamin A, Hoffmann-La Roche has, through research, developed a process for synthesis of citral from known or available chemicals. Detailed information regarding the synthesis is being withheld at present, but a report is to the effect that this synthesis is based on acetylene chemistry, and that an acetylene derivative provides a starting material.

By this process, the company can make vitamin A, beta carotene, ionones and methylionones, as well as linalool. The prices involved are in the pilot plant stage and patent applications are constantly being filed concerning the discoveries. It will be 1956 before Hoffmann-La Roche will be able to clarify its position regarding the use of these discoveries.

The synthesis of citral and vitamin A should eventually free the company of dependence upon the lemongrass crops of Guatemala and India and the uncertainty of nature and speculative conditions. The synthesis of linalool—one of the important products in perfuming—would adversely affect the market for Bois de Rose, the present source of linalool. Bois de Rose comes mainly from Brazil, and also from French Guiana. Linalool sells in the neighborhood of $6.00 to $6.70 per pound. Production of linalool, according to the U. S. Tariff Commission, was 251,000 pounds last year, and that of ionones and methylionones about 288,000 pounds.

Sixty Million for Drug Research

America's pharmaceutical industry is spending approximately $60 million a year for research, according to John A. McCartney, of Parke, Davis & Company. "New research laboratories have been built, or are planned, by practically every major pharmaceutical manufacturer," he told the American Pharmaceutical Association recently. "The reason is two-fold: First, the passing years amply demonstrate the fundamental

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soundness of a heavily-financed and adequately-staffed research installation. Second, research tends to be a self-perpetuation effort. Each new discovery opens new avenues of problem approach and new vistas of jobs to be done." He continued:

"It is not too much to hope that with adequate research investment—and in spite of the four-to-one gamble it represents—we will, in the immediate years ahead, see definite control or cure for some of mankind's most malicious diseases. Poliomyelitis appears to be high on the list of those diseases which will soon be controlled. The problem of the common cold and cancer will be solved. Heart diseases will no longer eliminate the high percentage of our mature population which it does today. . . . Leprosy, typhus, malaria and other world scourges are being rapidly controlled and may one day be merely textbook curiosities."

Sarcosinate Patent to Colgate

Colgate-Palmolive Company has been granted U. S. Patent No. 2,689,170, covering tooth pastes and similar preparations containing sodium N-lauroyl sarcosinate, the antienzymatic ingredient which Colgate advertises under the trademark Gardol. Colgate has used this chemical for about a year in their dental cream. Tests are reported to show that the sarcosinate remains active on the tooth surface for 12 hours or more, reducing the formation of acids that cause tooth decay. In clincal tests lasting for more than a year, persons using this product averaged 60 per cent fewer cavities, according to the company.

Colgate recently announced the establishment of a new radioisotopes laboratory for basic research in soaps, detergents, and toilet articles, and explained that research with radioisotopes had given direct evidence that the anti-enzyme, Gardol, remains in the mouth for many hours. Animal studies show that the chemical stays in the mouth more than 48 hours, according to Dr. Thomas H. Vaughn, Colgate vice-president in charge of research and development.

This research was carried out at the new laboratory at New Brunswick, N. J., by Dr. Manno F. Nelson. Gardol was first synthesized from radio-active carbon and the teeth of the test animals were then brushed with tooth paste containing the radioactive sarcosinate. Although the animals' mouths were thoroughly rinsed immediately, examination of their teeth for radiation showed that the sarcosinate was still present 48 hours after brushing.

Utah Court Voids Fair Trade

Utah's Fair Trade Act was declared unconstitutional late last month by District Judge A. H. Ellett in a suit brought by General Electric against a Salt Lake City retailer. The Judge declared that the Act was void and in direct contravention to Utah's constitution. While the decision is subject to appeal, the decision, if sustained, means that retailers may sell fair-traded products at any prices they wish, provided their profit is six per cent or more in accordance with the provisions of the State's Unfair Trade Act.

Abbott Laboratories recently obtained a permanent injunction restraining Schwegmann Brothers Giant Supermarkets, New Orleans, from violating Abbott fair trade contracts. The injunction covered not only over-the-counter items but also prescription products, whether sold in trade quantities or broken packages. Judge J. Skelly Wright handed down the decision. Schwegmann attorneys indicated no appeal would be taken.

Modern Pharmacy's 50th Year

Modern Pharmacy, one of the nation's first magazines to be published by a company in the interest of the profession of pharmacy, celebrated its golden anniversay with the September issue of this year. Parke, Davis & Company prints the slick-paper, full-color publication and distributes its bi-monthly to nearly 100,000 pharmacists and pharmacies in the United States, Canada, Puerto Rico and the Philippines. The first issue of Modern Pharmacy was published in September 1904.

A Doctor for Every 730 Persons

A ratio of one doctor for every 730 persons in the United States was reached during the past year through the graduation of the largest class of physicians in history and the continued expansion of medical schools, says the American Medical Association. The ratio will be lowered even more in the next few years as the number of medical graduates is expected to rise more rapidly than the general population. The record graduation of 6,861 doctors during 1953-1954 brings the nation's physician population to approximately 220,100.

Other highlights on medical education are:

An enrollment of 28,227 in medical schools sets a new record. Freshman enrollment of 7,449 is also a record. Of the freshmen entering medical schools, 68.9 per cent had "B" averages in their pre-medical training, 21.1 per cent had "A" averages, and 10.0 per cent had "C." Only 5.1 per cent of the freshmen left medical school because of academic failures or for other reasons in comparison to a 9.5 per cent rate 15 years ago.

Ten new four-year medical schools are in the construction or planning stage and will be in operation within the next five to six years. More than $76 million was spent during 1953-1954 for new facilities, remodeling, or completion of buildings for medical instruction. The budgets for the medical schools during 1953-1954 total more than $143 million. There were 21,328 physicians who did volunteer teaching without pay during the year to aid in educating medical students throughout the nation.

MCA Considers Health Research

The Manufacturing Chemists Association has under consideration the establishment of health research center to study the effects of chemicals on humans, according to MCA president, William C. Foster. The chemical industry has invested millions of dollars and man-hours in toxilogical research to determine the

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effects of chemicals on humans, said Mr. Foster. If a central research center is found feasible, the results from the correlation of existing data and of original research would be available. The sum of this research, said Mr. Foster, would make such an institution, "a benefactor to all mankind. Ideally such a research center would not be controlled by government or an individual company or a segment of the industry, but perhaps would be endowed by industry funds.

Lehn & Fink Viricide

Lehn & Fink have announced that a new disinfectant product that will, in five per cent solution, completely inactivate all three poliomyelitis viruses within ten minutes, and also destroy the influenza germ within one minute. The new viricide was developed ten months ago in the laboratories of Lehn & Fink's wholly-owned German subsidiary, Shelke Myer GM. BH., Hamburg, and is now being introduced on the German market. Called Gevisol, the product is put in water and used in cleaning woodwork, floors and utensils in hospitals and homes. It cannot be taken internally.

Dr. Morton Klein, Associate Professor of Bacteriology at Temple University, who has been conducting experiments with Gevisol, says it is a good germicidal agent. He describes it as an important addition to the list of compounds that can be used to kill polio viruses in sanitary work. Pointing out that it takes a strong germicide to kill the polio viruses, Dr. Klein indicated that Gevisol was not unique in its ability to destroy these viruses. He said that Lysol will not destroy them, but Chlorox will.

The product is said to have been approved by the Food and Drug Administration. Its effects will last for several days and there is a possibility that it might be used as a spray. The product has been the subject of intense market research by Lehn & Fink. It will be marketed as soon as the results of this research can be evaluated, and the company can decide whether to market the product as a proprietary or ethical preparation.

Must Offer Allowances to All

Unless a manufacturer informs all his retail customers regarding advertising or other allowances or discounts which he is granting to one or more of his customers, he is violating Section 2(d) of the Clayton Act as amended by the Robinson-Patman Act.

This was the ruling of the Federal Trade Commission in the case of Kay Windsor Frocks. The FTC order was based on findings that the respondents had granted to some customers credits or payments in consideration for advertising services but that credits or payments for such services were not available on proportionately equal terms, or available at all, to others competing with such customers. The heart of the opinion as given by the Commission, reads:

"Although the word 'available' rather than 'offered' appears in the relevant subsection of the Act, the statute contemplates that customers competing in the resale of a seller's merchandise be afforded equal opportunity to share in payments for promotional services in the event the seller elects in the first instance to provide it to one of their competitors. A course of conduct under which a seller fails to inform respecting such compensation or make known his terms or otherwise to offer them to one customer while granting payment for services to his rival reseller essentially represents concealment. In such case, the credit or allowance is not 'available' to the unfavored competitor, for all practical purposes a withholding and denial of opportunity to share occur, and the law is violated."

Cosmetic Chemists Hold Seminar

The first seminar of the Society of Cosmetic Chemists was extremely successful. The facilities available at the Academy of Science in New York were taxed to the utmost and all reservations were sold out some time before the seminar was to be held. Three subjects were covered in the two-day meeting, and plant trips were held on the afternoon of the second day. The first subject covered was that of Emulsions in Theory and Practice; the second was Animal and Human Testing of Cosmetics; and the third was Hair Structure and Permanent Waving. Much time was allowed for free discussion of the three subjects. There will be no publication of the discussions at the seminar since it was felt that this would lead to much freer discussions.

Fair Trade Being Evaluated

"More and more manufacturers are recognizing their stake in making fair trade work to safeguard their valuable trade-marks and their mass distribution systems from the destructive effects of price-chiseling," according to John W. Dargavel, chairman of the Bureau of Education on Fair Trade. As instances of this trend, Dr. Dargavel cited the vigorous fair trade enforcement activities of leading manufacturers in different fields. For example, the Magnavox Company has canceled the franchises of its some 1,600 dealers and will re-franchise only those dealers who respect the company's fair trade prices. Also, in five weeks the Lionel Corporation obtained eighty injunctions against fair trade violators in just one New Jersey county. Lionel has stressed that unless the discount house threat to established retailers is contained, the slump in orders will endanger manufacturing stability and lead to "substantial layoffs at the manufacturing level," as well as to injury of the value of the manufacturer's brand name. Others cited by Dr. Dargavel are Sunbeam Corporation and General Electric. Sunbeam has over 200,000 signed fair trade contracts with its dealers, and General Electric has initiated over 370 legal actions in 14 states since 1952.

"These and other manufacturers are demonstrating their belief that indiscriminate price-cutting and price-chiseling lead only to economic chaos, destroying the consumer's standards of value, wiping out legitimate retailers and touching off the vicious spiral of falling sales, unemployment and depression. Effective fair trade plays a major role in safeguarding our sensitive brand-name, mass-production economy from these perils," said Dr. Dargavel.

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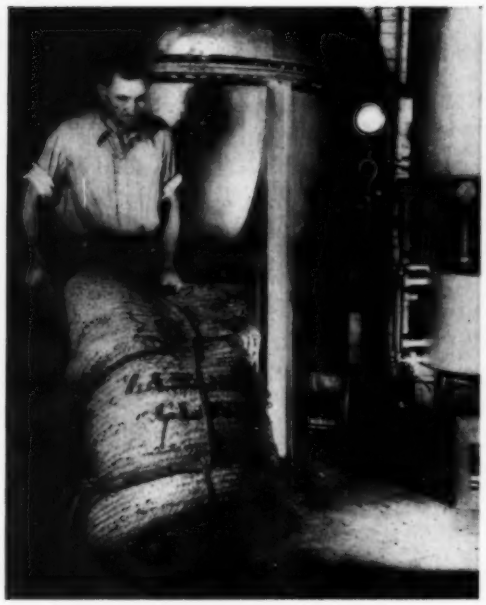

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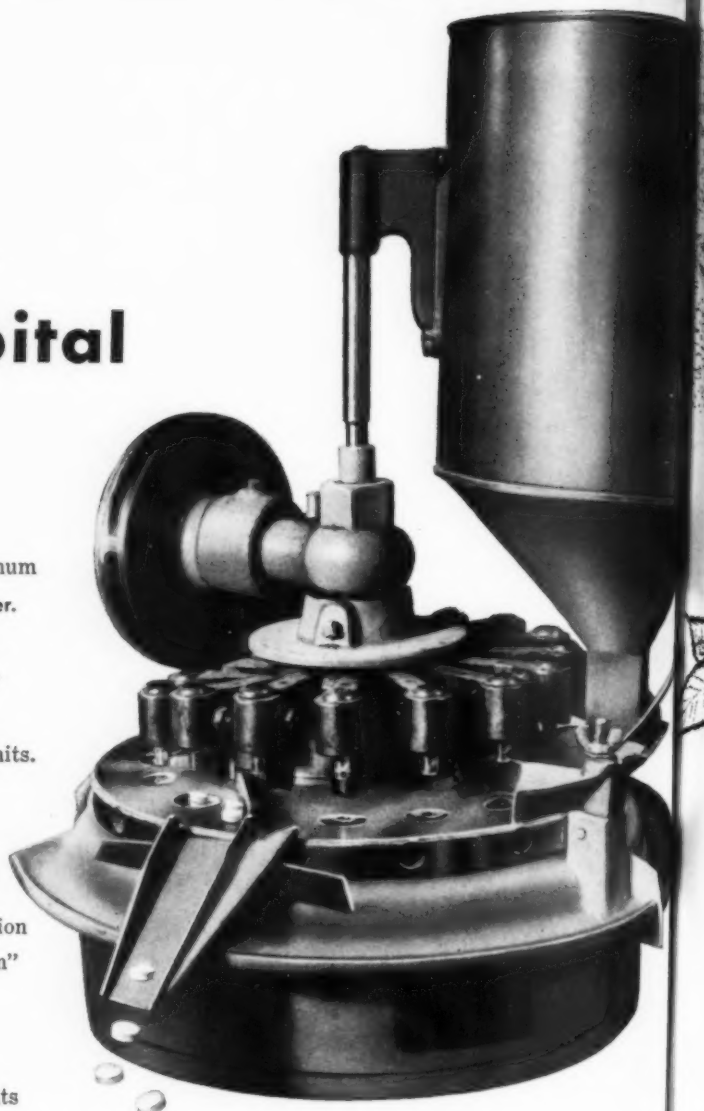

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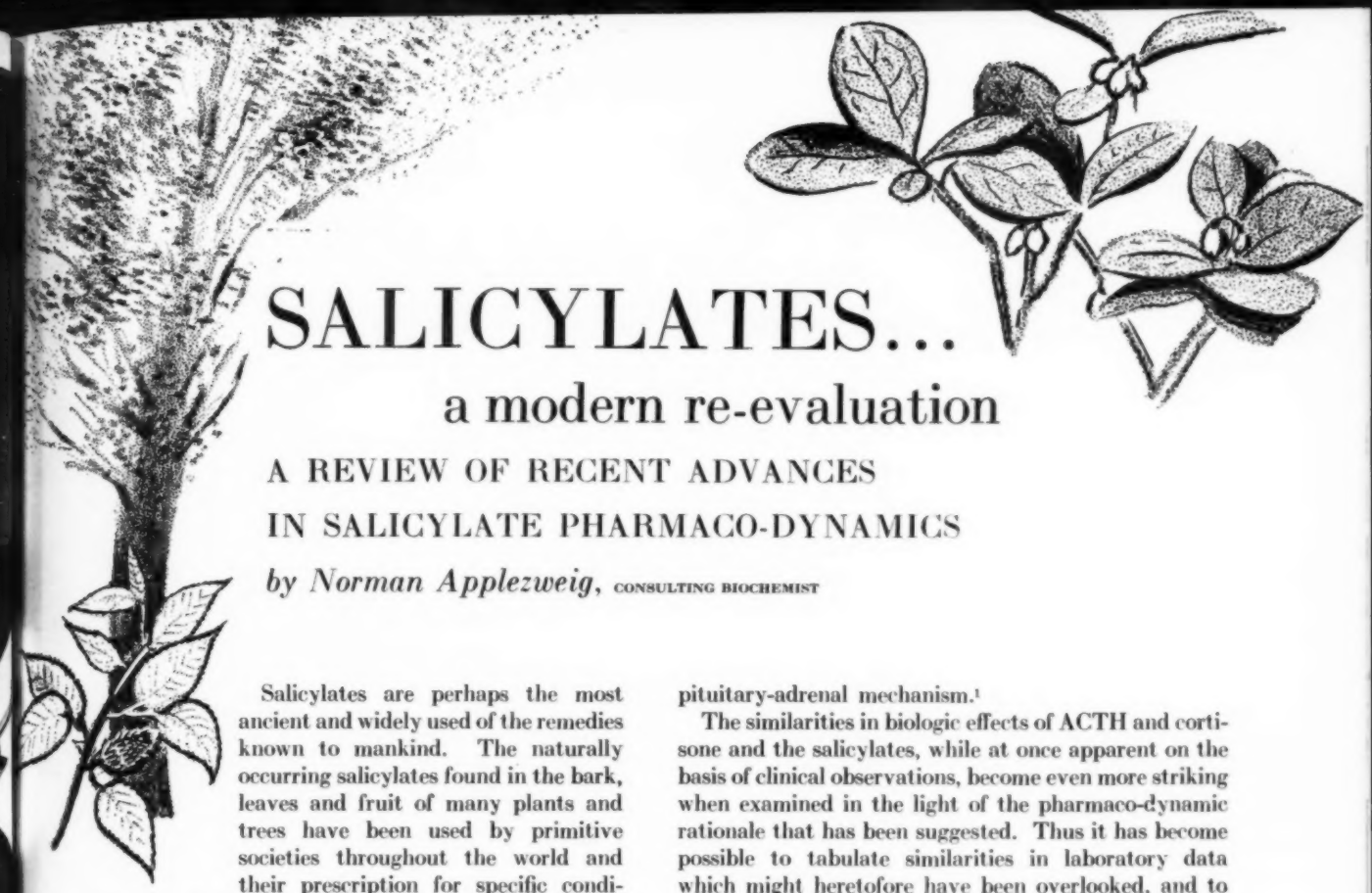


SALICYLATES...

a modern re-evaluation

A REVIEW OF RECENT ADVANCES IN SALICYLATE PHARMACO-DYNAMICS

by Norman Applezweig, CONSULTING BIOCHEMIST

Salicylates are perhaps the most ancient and widely used of the remedies known to mankind. The naturally occurring salicylates found in the bark, leaves and fruit of many plants and trees have been used by primitive societies throughout the world and their prescription for specific conditions may be found in the earliest records of medical history.

In the more than 2,000 years since Hippocrates recommended the leaves of the willow tree as an analgesic in childbirth we have greatly increased our knowledge of when and where to use the salicylates and how to produce them in unlimited quantity through synthesis. We can agree with the judgment of the ancients that salicylates are remarkably effective drugs. But our knowledge of how or why they work has remained virtually at a standstill until recently.

The development in the last few years of completely new concepts concerning resistance to disease has led to a re-examination of the problem of salicylate action. The result of this new look at an old problem has added greatly to our understanding of modern therapeutics and helped to explain the ancient mysteries concerning the effectiveness of the salicylates.

The discovery of the anti-inflammatory properties of ACTH and cortisone by Drs. Kendall and Hench, has been hailed as the start of a great new era in medical history. The physiologic facts, which were disclosed as a result of the discovery and employment of these hormone products, furnished great insight into the pathology of arthritis and other stress conditions, and focussed a new and important light on the pharmacodynamics of anti-inflammatory therapeutic agents.

Before the cortisone-ACTH era, salicylate therapy was one of the most effective means of managing rheumatic fever and arthritis. It was most reasonable, therefore, that the question should have been raised as to whether or not salicylates operate through the pituitary-adrenal mechanism.[1]

The similarities in biologic effects of ACTH and cortisone and the salicylates, while at once apparent on the basis of clinical observations, become even more striking when examined in the light of the pharmaco-dynamic rationale that has been suggested. Thus it has become possible to tabulate similarities in laboratory data which might heretofore have been overlooked, and to test the rationale by experimental techniques which confirm and explain what were previously only surmises.

One of the earliest suggestions that the activity of salicylates may be due to the stimulation of the adrenal cortex causing a liberation of corticoid substances, was made by Calesnick and Bentner in 1949.[2] Robinson[3] reported that adrenal cortical stimulation, as judged histochemically, could be demonstrated in rats. This work was stimulated by the observations of Cochran[4], that aspirin can produce signs of mild Cushing's syndrome. Bertolani, et al[5], confirmed that salicylates stimulate adreno-cortico function, by observing that in guinea pigs there is an increase in the excretion of urinary 17-keto steroids and a decrease in circulating eosinophils.

Further confirmatory evidence was supplied by the experiments of Cronheim, et al[6], who demonstrated that salicylates and a number of substituted salicylic acids cause a significant depletion of ascorbic acid and that this may be prevented by hypophysectomy. The experimental facts which had accumulated by this date strongly indicated a specific direct or indirect action of salicylic acid on the anterior pituitary, which results in the production or release of increased amounts of adreno-corticotropic hormone.

Roskam and Van Cauwenberge[7] summarize their own experimental and clinical findings as of the end of 1952 in the following way. They feel that it has been established experimentally that (1) the injection of salicylates entails the same biochemical, hematologic and histologic consequences as the administration of

(*Continued on page 557*)

Adequate and Properly

The drug manufacturing industry depends mainly upon pharmacists for the distribution of its products. Without pharmacists there could be no drug stores—no one to fill prescriptions. During the present period, when prescription products and so-called ethical preparations are the main consideration of the industry, a plentiful supply of well-educated pharmacists is an essential requirement for the welfare of the industry. Because of the sharp increase in recent years in the number of prescriptions filled, and in the sale of ethical preparations either prescribed or recommended by physicians, the number of pharmacists needed has increased sharply, and the type of education which they must receive has become of increased importance.

But not only does the drug manufacturing industry require pharmacists for the distribution of its products, it also needs them in its own individual companies for any number of reasons.

Due to the fact that education is costly, it is well known that tuition fees cannot be placed high enough to support any college. And even though the tuition fees are far below the total cost of educating a student, many young men and women desiring to follow careers in pharmacy—as well as in other professions—often cannot even afford the tuition fees which are charged.

In order to have in this country an adequate supply of pharmacists, it is essential to have sufficient facilities to educate them. And these educational facilities must be supported by someone. Although the schools of pharmacy have largely been part and parcel of the larger universities, and have received heavy support from the general educational funds of these universities, the drug industry was finally forced to the decision that it must undertake support of these institutions in a real way as a means of self-preservation.

The necessity of supporting the colleges of pharmacy in this country was recognized by the National Drug Trade Conference during the dark days of the depression of the thirties. For five years a committee on contributions to schools of pharmacy studied the basic problem and reported back each year to the Conference—a group which represents every phase of pharmacy—education; professional and retail practice; wholesaling; drug, proprietary, pharmaceutical, and chemical manufacturing. And out of these studies and reports there came the plan that eventually led to the incorporation in 1912 of the American Foundation for Pharmaceutical Education.

To give an idea of the type of organizations which were considering this problem, we list the members of the National Drug Trade Conference which gave birth to the Foundation. These members are: The American Association of Colleges of Pharmacy; American Drug Manufacturers Association, American Pharmaceutical Association, American Pharmaceutical Manufacturers Association, Federal Wholesale Druggists Association, National Association of Boards of Pharmacy, National Association of Chain Drug Stores, National Association of Retail Druggists, National Wholesale Druggists Association, and The Proprietary Association.

The principal objectives of the American Foundation for Pharmaceutical Education are: (1) to provide adequate, well-trained, and reliable personnel to man the retail pharmacies of the country; (2) to furnish the pharmaceutical industry and allied manufacturing concerns, hospitals, government agencies, college faculties, and other professional fields with technically and scientifically trained personnel; (3) to help colleges develop strong undergraduate programs; (4) to support graduate work in colleges qualified to carry out such programs; and (5) to encourage scientific research, both as a necessary component of graduate work, and as special projects.

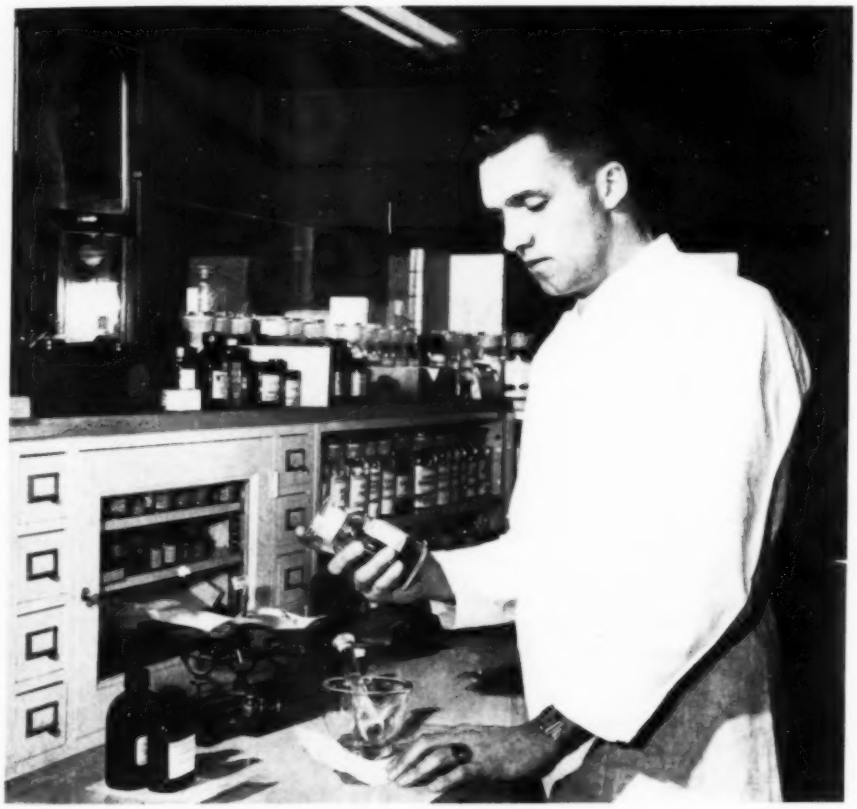
These diverse activities of the Foundation for a strong profession through education are made possible by the continuing efforts of the Foundation's members, directors, officers, and committees, as well as the generous support of its patrons.

Administrative and management authority of the Foundation is vested in a Board of Directors composed of thirty leaders from every branch of pharmacy. These men are from the fields of proprietary manufacturing, pharmaceutical manufacturing, colleges of pharmacy, chain stores, wholesale druggists, and other related fields. Every one of these men is deeply interested in the problem of pharmaceutical education and they give liberally of their time and talents.

All allocations of educational funds, selection of graduate fellows and teaching fellows, and authorization for undergraduate scholarship awards are made by the Board of Grants. This is composed of four members, two of which are outstanding men in pharmaceutical education, and two are outstanding representatives of the pharmaceutical manufacturing industry.

Because colleges cannot exist without teachers, assurance of a steady flow of properly trained men for

Trained PHARMACISTS



FREDERIC LEWIS PHOTO

this profession became one of the problems which the Foundation has had to face. This problem was heightened by the fact that the annual university output of all Ph.D.-trained scientists is diminishing to about half the number graduated in 1950, and this occurs at a time when the industry demand is increasing. To help meet this problem so far as the demand for doctors in pharmacy, pharmaceutical chemistry, pharmacology, and related fields are concerned, the Foundation initiated a graduate fellowship program in 1946. Upwards of three hundred fellowships have been awarded, but the colleges and industry absorb these scientists as fast as they are graduated, and there is no lessening of demand. Therefore, the Foundation continues to allocate more than half of its annual budget for graduate fellowships. On the average, the Foundation receives four times more applications from highly qualified and deserving men than can be assisted with available funds. Although expansion of this program when income permits is highly desirable, it has already strengthened the faculties of our colleges and added productive workers to the industry's laboratories.

To meet an especially urgent need for teachers in the business subjects of pharmacy, the Foundation, in 1952, initiated a new program of teaching fellowships in business administration. Under this program, the Foundation contributes one-half of a pharmacy teacher's salary (up to $3,000 a year) in order that selected men may devote half their time to study in graduate schools of business administration and thus become qualified as teachers of pharmacy administration for our colleges.

(Continued on page 551)

the SUNTAN

part two how much

EWING GALLOWAY PHOTO

The question, "how much protection should be built into a sunburn preventive?," might be accompanied by an allied implication—why should the skin require any artificial defense from a force as natural and omnipresent as sunlight? Man has lived in an environment of solar radiation from the very commencement of his long evolution. From the single cell to the infinitely complex creation that he is today, the sun's rays have been an integral phase of his universe, supplying light, heat and photo-chemical energy. Obviously sunshine is beneficient yet witness the millions of dermatologic injuries annually wrought by this friendly and vital radiation. Man's shield against the outside world, the skin, is apparently incompetent in defending itself from the harmful effects of the solar spectrum. Further reasoning reveals the defect lies with Man and not the design of his integument. In the original scheme of things, it was intended that Genus Sapiens be an outdoor creature. Throughout adolescence and adulthood, many days each year would be spent in the sun, during which his skin would become slowly and deeply immunized against excess insolation. These defense mechanisms, because of their depth and density, would be carried over the long sunless winter into the spring when solar radiation is again potent. The immunity acquired during the previous summer, although somewhat reduced, is still sufficient to prevent burns during the first ex-

INDUSTRY *by L. Stambovsky*

protection

posures in early spring. As the new season advances, the entire cycle of building and storing resistance is repeated. Under such conditions sunburn was unknown. A classic example of complete indifference to solar radiation, was the American Indian before the white man taught him to wear clothes. Life guards and others engaged in outdoor occupations have in some degree gained a similar resistance.

Modern living has radically changed Man's relationship with the environmental media in which we exist. Man has built himself an indoor world and has become a stranger to his oldest companion and benefactor, the sun. The average person spends one or two weeks annually outdoors and perhaps a few weekends. The insignificant number of hours of irradiation that could be obtained within such periods are totally inadequate to stimulate those agencies which close the door against injurious radiant energy. So far as carrying this trivial, if any, defense over to the next year is concerned, it can be completely discounted. This means, that the average sunbather, during the initial exposures of the new season, presents to the sun a practically defenseless skin. Why should sunlight be malicious even under the described circumstances? For the simple reason that the sun must supply a myriad of living things with variable amounts and types of radiant energy. It cannot differentiate for individual organisms, either qualitatively or quantitatively. Each must be able to choose its own particular requirements and exclude excess. Civilization has deprived Man of this ability and consequently we note as regularly as time and tide, millions of painful and destructive solar burns.

Sunburn Can Be Prevented

The person who is sensible and far-sighted enough to want to prevent photochemical damage to his skin must resort to one of two alternatives; either restrict exposures to within non-injurious tolerance or use a sunburn preventive. Voluntary control has not been and probably never will be successful. This is fact because of several reasons; first neither the public nor the physician has any idea of what constitutes a safe irradiation for average skin. Second, after a long dreary, sunless winter, it is almost impossible for the layman to associate danger with the warm, relaxing, pleasurable sensations stimulated by sunlight. Even if aware of certain injury, many persons would still ignore same by virtue of the enjoyment of the moment and their limited total time available.

Dermatologic Reactions to Selective Wave-Lengths of Ultra-Violet Energy

The physics of radiant energy is extremely complex and voluminous. That division of the spectrum of interest herein, the ultra-violet, is in itself highly involved and tedious. Therefore we shall employ only the irreducible minimum data bearing upon the subject in question. Solar ultra-violet energy extends from 2950 Angstroms, (actually nearer 3000A.) to 4000 A., the visible wave-lengths commence at 4000 A. This entire region is of interest and relevant. The erythemogenic or burning rays

occupy but a small section of the ultra-violet spectrum—between 2967 A. and 3130 A., as can be seen in table 3.

Table 3
RELATIVE EFFECTIVENESS OF ULTRA-VIOLET ENERGY OF DIFFERENT WAVE-LENGTHS IN PRODUCING ERYTHEMA AND TAN

Wavelength Angstroms	Erythemal Effectiveness "International Commission on Illumination"	Tanning Effectiveness Luckeish and Taylor
2967	1.00	1.00
3022	0.55	0.50
3130	0.03	0.02
3342	0.000	0.004
3663	0.000	0.0012

Luckeish believes that for energy longer than 2950 A., the spectral erythemal effectiveness curve and the pigmentogenic effectiveness curve are identical. It can be further noted in Table 3 that energy above 3130 A. is practically devoid of any capacity to produce erythema or irritation. This is of keystone significance. Luckeish and Taylor[7] found two strong tanning lines at 3342 and 3663 Angstroms which give rise to direct or immediate pigmentation with slight, if any, visible irritation. These two wave-lengths were generated by a quartz mercury arc which of course is characterized by a discontinuous spectrum. Sunlight in these regions radiates a continuous spectrum and quite probably all the lines in the vicinity of those quoted are pigmentogenic. Other investigators support this view. Without proceeding further, sufficient evidence has already been presented to show that there are rays of the sun which tan without burning. Further desirability of the actinic energy above 3200 A. is borne out by Luckeish: an irradiation with an artificial source of of ultra-violet with the energy density on the skin at 9 microwatts per sq. cm. at 3342 A. and 6500 microwatts at 3663 A., produced a direct moderate tan without visible erythema. Noon sunlight in July in the spectral region 3300 A. to 3800 A. would have about half the tanning effectiveness of the radiant energy which produced moderate tanning in this experiment. Therefore, in sunlight an immediate and direct tan could be obtained by a 150 irradiation, (twice 75 minutes), *proriding* the effect of the erythemogenic or burning rays between 2967 and 3130 Angstroms could be rejected sufficiently to avoid a severe burn. From the Luckeish erythemal data, it is known that 100 minutes of June sun on average untanned skin, will provoke a painful burn and 200 minutes a blistering burn. An irradiation of 150 minutes will fall in effect somewhere between these two stages.

The writer conducted a limited study which serves to confirm the direct tanning phenomenon. Subjects were given a preparation which contained a screen transmitting all energy above 3200 A. but which absorbed practically all energy below 3200 A. Under the Florida sun during April at peak hours, exposures of four to six hours were requested and supervised. Observations were made after termination of irradiation and also several hours later. In every instance there was the unmistakable presence of varying degrees of tanning, with slight or no erythema. Hausser[8] reports a tanning or browning immediately after exposure to energy in the region of 3650 A. Henscke and Schulze[9] have made exhaustive investigations along these lines. Their work encompassed not only experiments with artificial radiant energy but also with filtered sunlight. They found that with mercury arc spectra of the frequencies 3130, 3190, 3350 and 3550 Angstroms, direct pigmentation could be observed immediately after exposure without erythema. Identical reactions were recognized after exposures to filtered sunlight, wherein only energy between 3200 and 400 Angstroms was allowed to reach the skin. According to this research, direct pigmentation with slight if any erythema is a function of the region between 3200 and 4300 Angstroms, with a peak at about 3400 A. They further state that irradiation with frequencies above 3200 A. may be indulged with impunity and without fear of unpleasant repercussions.

The foregoing indicates strongly that the only wave-lengths of ultra-violet energy from which vulnerable skin should be protected are those between 2967 and 3130 Angstroms. This region must *(Continued on page 534)*

Employee Suggestion Systems in the Pharmaceutical Industry*

A DISCUSSION AND REPORT ON AN INDUSTRY-WIDE SURVEY

by George M. Naimark, Ph.D.

WHITE LABORATORIES, INC., KENILWORTH, N. J.

It might be well to initiate this discussion with two warnings: suggestion systems—or any other single corporate activity—cannot be panaceas for the ills which have their basic origins in other operational areas; and secondly, a suggestion system which is hurriedly and casually instituted without adequate consideration of the factors necessary for successful operation is almost certainly doomed to failure.

Successful suggestion systems, on the other hand, are powerful management tools and their value is now well-known. In order to determine the frequency of use of such systems in the pharmaceutical field, as well as pertinent operational details, an industry-wide survey was conducted. Sixty-one questionnaires containing 32 questions were sent to all of the large and most of the medium-sized pharmaceutical concerns. Of the 61 questionnaires distributed, 48 replies were received for a 78 per cent return. Of those responding, 18 companies, or 37.5 per cent, have employee suggestion systems now in operation. Two companies reported the previous abandonment of unsuccessful suggestion programs. The detailed results of the survey are included in the subsequent discussion.

General

The majority of the suggestion systems in the pharmaceutical industry were initiated after the start of World War II: six before 1941 and twelve after. It is interesting to note that the year 1941 represents the turning point in American industrial experience with suggestion plans; it has been reported that up until Pearl Harbor only five per cent of all suggestion systems in the United States were successful.[1] However, the survey shows that currently the pharmaceutical industry considers its idea programs quite effective, as is seen from the following self-rating summary:

Excellent:	4
Good:	11
Fair:	2
Poor:	0

*The survey was conducted by the author while at Strong Cobb and Co., Inc., Cleveland, Ohio.

He thought of a better way

Courtesy Abbott Laboratories

In June, 1942, a national non-profit organization was founded to encourage suggestion system activity in industry, commerce and finance, and government agencies. This organization, which is known as the National Association of Suggestion Systems, or NASS, now has a membership of over 850. There is much to be gained by joining this group (headquarters located at 122 South Michigan Avenue, Chicago 3, Illinois); some of the benefits are listed below:

(1) Access to the NASS library and Service Exchange to obtain the experience of companies operating successful plans.
(2) Receive the NASS Quarterly and the Suggestion News Letter.
(3) Receive supplements, surveys and statistical reports.
(4) Receive analyses of various successful plans.

Ten pharmaceutical companies now share the benefits of membership in NASS, including: Bristol Laboratories, Lilly, Abbott, Mead Johnson, Squibb, Johnson and Johnson, Parke-Davis and Merck.

(*Continued on page 555*)

COURTESY TUSSY COSMETIQUES

Make-up

The evolution of the make-up base to the more popular present forms represents a rather interesting study in the general technical advances made in cosmetics over a period of some fifty years. Its beginnings were initiated because it was felt that face powder by itself, though a satisfactory covering agency when freshly applied, did not adhere as well as desired and in addition did not offer as smooth a finish as was desired by some. The early attempts at make-up bases were therefore preparations designed to enhance the results produced by face powders. As time went on there was a further trend to incorporate into a single preparation both the functions of a make-up base and a face powder as well. In their present forms the make-up bases are designed as dual functional products, in which the powder and the rest of the vehicle are designed to impart both the desired matte finish and the desired coverage and pigmentation as well.

The early bases were designed to add a thin layer of oil to the face so that the face powder subsequently applied would adhere in a better fashion. These preparations consisted primarily of vanishing types of creams in which perhaps a slightly higher concentration of oil was used than usual. A later innovation was the use of the same type of vehicle in which was incorporated relatively small amounts of titanium oxide and pigments. The first of the modern make-up bases, is generally conceded to be the product which resembled a compact face powder but which was applied with a moist applicator. This type of base is still quite popular and represents a reversal in the trend up to its inception, since it consisted of perhaps about 70 per cent of pigments and powders, and perhaps 30 per cent of emulsifiers, humectants and oils. It could be really thought of as a dehydrated vanishing cream with pigments and powders incorporated. Indeed, the first of these pro-

duced was made by first forming a cream incorporating the powders and fillers, and then drying as the mass was then ground and pressed into its compact form. Most manufacturers, however, did not utilize this method of manufacture, but incorporated the water soluble ingredients in the humectant and added them to the powder in this fashion and then added the lipophilic portion of the base. With the development of improved methods of grinding of powders it became possible to blend the various ingredients almost as intimately as a pre-cream forming process. Elimination of the drying process not only reduced this production cost but greatly helped in keeping the color control at a desired level.

This product was essentially a powder, but contained enough humectant and emulsifier to cause ready emulsification of the oils with the addition of water by means of the moist applicator with a mechanical inclusion by this means of trituration of the pigments and powders. This foam enabled the user to apply a film which, when it dried, produced a more uniform and smoother covering than was possible with the usual face powder.

Following the new trend started by the cake make-up, attempts were made to eliminate the wet applicator method of application. A brief flurry was started by the incorporation of the powders in a completely oil vehicle. The oil had a low viscosity and therefore was capable of application in an extremely thin film. Such a film was made possible by the use of substances such as isopropyl myristate and similar esters of low molecular weight monohydric alcohols. A parallel development was much the same type of preparation, this time in a compact form. It was formulated by the introduction of enough carnauba wax or other high melting point wax to cause the preparation to stiffen after having been poured into its containers when still hot and liquid. These preparations were well thought out and they actually did impart a smooth highly adherent film to the face. However, they were not too well received. It may be that the consumer objection was the result of too oily a feeling after application even though the appearance may have been satisfactory, but under any circumstances they gave way to a further development which is still highly popular.

This newer form is a liquid emulsion type of preparation where the pigments and fillers are suspended as part of the emulsion, thus forming an homogeneous system, readily pourable and readily applied. There is present a minimum of 20 per cent of powders and pigments, a large proportion of which is titanium dioxide, making it possible to procure the desired covering and pigmentation properties. These pigments and fillers are incorporated in what is a liquid lotion system containing an emulsifier and other suspending agents as well as oils. Since water is the major constituent of this system we are afforded a medium which is plastic enough to be readily applied, and its film after evaporation is essentially a powder film with which enough oils are incorporated to impart the desired degree of adhesiveness. By the very nature of its application

Bases *by Harry Hilfer*

the matte finish is also readily achieved and is capable of producing the sought after effects. When properly formulated, the dry film may also be made highly impervious to moisture, and, what is more important, it will have none of the properties which would classify it as being oily or greasy.

This type of base has been on the market long enough now, and has been popular enough for us to assume that it is a permanent addition to the cosmetic counter. It is very interesting since this type has been, I think, the first liquid emulsion form of cosmetic preparation which has been able to support within itself so high a concentration of powders and pigments. Its evolution was a gradual one made possible only by the development during a fairly recent period of a large number of synthetic emulsion stabilizers which are in general use in its formulation. There are several different approaches from a technical standpoint to the synthesis of such a system. They depend on first forming a somewhat stiff emulsion which may be liquified further by the introduction of the suspending agencies and powders, or by the use of relatively large amounts of emulsifying agents which in themselves would introduce a suspension medium, or by the use of hydrophylic silicates which are readily dispersed in water and aid in the suspension of other powders present. In many cases all methods are used in a single system. Much of the work that has been done on these products are trade secrets. Certainly it is not the purpose of this article to discuss their technical aspects except in the broadest terms. Therefore no mention will be made of any of the specific materials used in formulation of these systems.

I think they can best be described as well balanced hydrophylic-lipophylic emulsions designed so that

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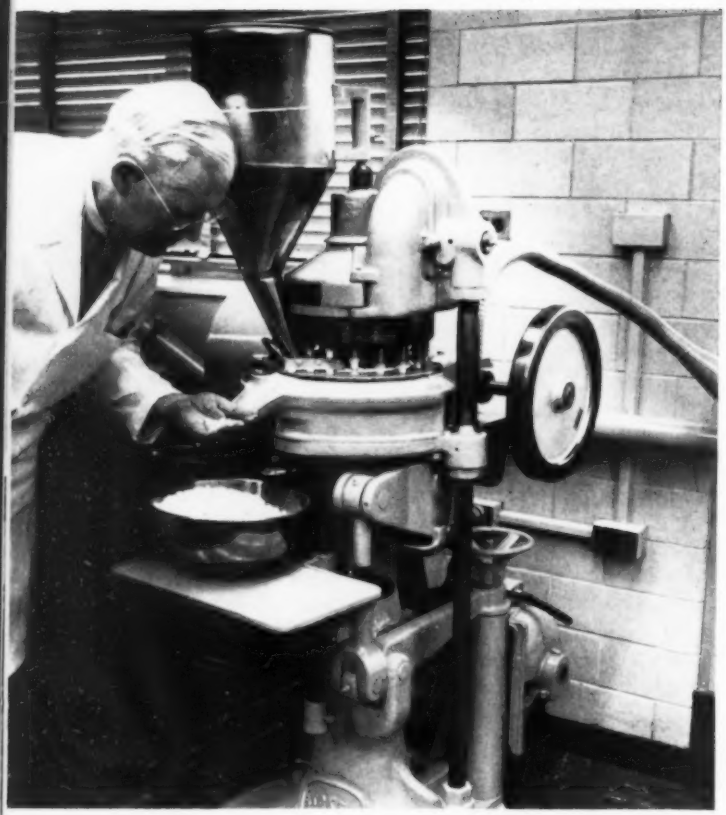


COURTESY SHARP & DOHME, INC.

Problems in Producing

by Leonard Charkin
ASS'T PROFESSOR OF PHARMACY
COLUMBIA UNIVERSITY COLLEGE OF PHARMACY

Compressed tablets are commonly prepared by one of three methods or some modification of these. They are: direct compression, wet granulation, and slugging or double compression. Direct compression is applicable only to that handful of materials which will form perfect tablets without prior treatment of any kind. The process is effective with those materials which, because of their physical nature are normally cohesive enough to bind under pressure and form satisfactory tablets. Such materials as sodium and ammonium chlorides, some iodides and bromides, methenamine and potassium permanganate are examples of this class of substances.

The aim of the other two processes which require some treatment or processing of the powders before compression is to obtain the tablet components homogeneously dispersed in granular form. It is important that the material to be compressed be in the form of free-flowing, relatively uniform granules since the compression machines rely on volumetric gravity fill to achieve uniformity in dosage. Thus each die fill must be constant in order to assure proper dosage.

Homogeneity of the dispersion of each of the tablet components throughout the mass is obviously the first important characteristic to be achieved regardless of the granulating process used. This must be assured prior to the granulating step and can usually be accomplished satisfactorily through the intimate mixing of the finely powdered tablet components. The particular machine used for this operation depends upon the nature of the materials involved and the concentration of each of the components in the mass. For most mixtures of relatively free-flowing, finely divided powders the use of a dry powder blender for this mixing operation is adequate.

However, if it is necessary to achieve a uniform dispersion of a small amount of active ingredient throughout the mass of powders, the dry powder blender will be found inefficient since it would require too much time to accomplish its purpose. In other instances such as the dispersion of a solution of a color throughout the powders or the mixing of materials of different particle sizes a similar situation arises.

The solution to these problems is generally found in the use of a mill to accomplish rapid and thorough dispersion. A hammer mill such as the Fitzpatrick Comminuting Machine or the Mikro-pulverizer is generally most efficient. Some mixtures may require pre-mixing in a dry powder blender before passage through the mill since the mill will process only a small portion of the mass at any one instant. In the handling of small quantities of potent or costly materials, a primary dilution can be made using a jar mill.

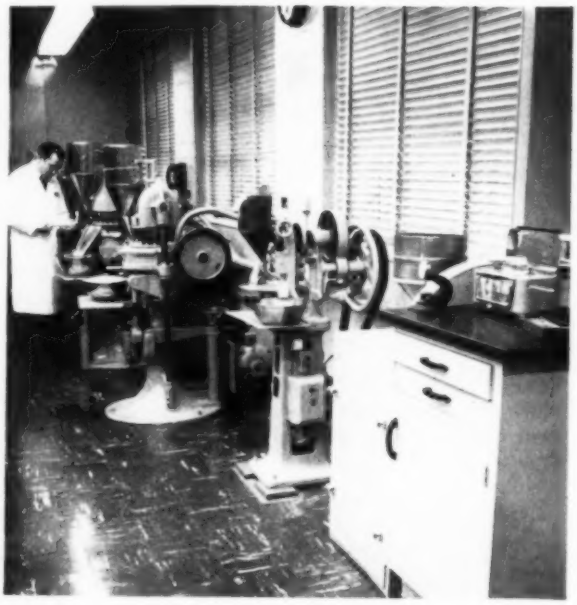
Wet Granulation

The wet granulation process, currently the most widely used method for the preparation of granules for tablet compression, accomplishes its purpose through the use of a material, known as the granulating agent, which causes the powdered tablet components to aggregate. This aggregation is brought about by the bonding properties of the granulating agent which is usually an adhesive in solution or a material which by its solvent properties on one of the tablet components, bestows adhesive properties on the mass of material.

The majority of tablets are composed of a mixture of powdered materials formed into granules by one of

* Presented before the Engineering Seminar, Chas. Pfizer & Co., New York, May 27, 1954.

Compressed and Coated Tablets*



COURTESY SHARP & DOHME, INC.

the two methods. The strength of the bond between the individual powdered particles in the granule is the critical factor which determines the quality of the finished tablet. In the wet granulation process the nature of this bond is governed by a number of factors including the nature of the granulating agent, the distribution of the granulating agent throughout the mass and the extent to which the granulating solution wets each of the powdered particles.

There is currently no objective method for the measurement of the extent of this bonding. Empirical means are used exclusively. Thus the terms, "hard" or "soft," applied to granulations, refer to the extent to which this bonding has taken place.

Actually the final criterion which is used to measure this bond is the hardness value of the finished tablet. The granules which are formed must be sufficiently hard to resist crumbling when subjected to compression in the tablet machine. Thus the tablet is formed by the plastic deformation and intermeshing of granules of various sizes and shapes upon the application of pressure, and not by the crumbling of the granules under pressure.

If this crumbling takes place to any extent it is an indication that the bond among the powders which aggregate to form the granules is not sufficiently strong. The result is a tablet which is too friable, chips easily and laminates or "caps" under pressure; or simply a tablet which falls apart after ejection from the compression machine.

If such tablets are examined closely it will be discovered that they are no longer composed of distinct granules, but have reverted almost entirely to fine powder particles. The screening and recompression of such tablets is usually a futile task since the primary fault, the weak bonds within the granules, has not been remedied.

Let us examine this situation closely since it is the most common problem encountered in the preparation of compressed tablets by the wet granulation method. The major factor which influences the bonding within the granule is the extent to which the granulating solution wets each of the particles of powder. In general, the many materials which are used as granulating agents are sufficiently adhesive to effect adequate bonding. Acacia, tragacanth, gelatin, starch paste, syrup, liquid glucose, or any of the other adhesives which are commonly used have sufficient binding power to granulate practically any material used in tablet formulas. Yet there are many instances where the use of high concentrations of these materials fail to produce satisfactory granules.

The fault lies in the extent to which these granulating agents reach and wet each of the particles within the mass of powders. The first insight into this was had when it was observed that granulating agents were more efficient when added in solution than when incorporated dry into the mixture of powders. Each of the particles has a coating of adsorbed air on its surface, and it is this film which must be penetrated before the powders can be wetted by the granulating solution. Of course all

(*Continued on page 559*)

Lyophilized Pharmaceuticals

by Herbert M. Gross, Ph. D.

HEAD, PHARMACEUTICAL DEVELOPMENT DEPARTMENT, PHARMACEUTICAL RESEARCH DIVISION, COMMERCIAL SOLVENTS CORPORATION, TERRE HAUTE, INDIANA.

Many articles have been published concerning the physical manifestations of freeze drying [1,2,3,4,5,6,7], numerous patents have been recorded on the development of lyophilizing apparatus[8,9,10], an abundance of freeze drying units has been described[11,12,13,14], reviews and books have been prepared[15,16,17], and articles and patents have been written adapting this process to food[18,19,20,21], biologicals[22,23,24], and pharmaceuticals[25,26,27]. However, little technical data has been written regarding techniques of processing and formulating pharmaceutical products.

Essentially, freeze drying is a type of vacuum drying process adapted to preserve relatively unstable substances so that they retain their original value over periods of time which would otherwise impair or destroy their useful characteristics. This process retains the original volume of the frozen material and permits rapid reconstitution with aqueous diluent. Many unstable biologicals and pharmaceuticals are prepared by this process. Freeze drying consists of rapid freezing of aqueous solutions and the subsequent sublimation of ice under vacuum. Evaporation under vacuum is accomplished at such temperatures that heat sensitive products are not adversely affected.

More detailed descriptions of objectives, basic principles, and equipment applications are found in articles by Flosdorf[16] and Guess and Burlage[17].

A study of the formulation, processing, assay and stability of various pharmaceuticals has revealed several fundamental concepts concerning these lyophilized products. Quality of the final product, characteristics of the lyophilized plug, drying cycle determinations and equipment control are of interest to producers of lyophilized pharmaceuticals and enter into this discussion.

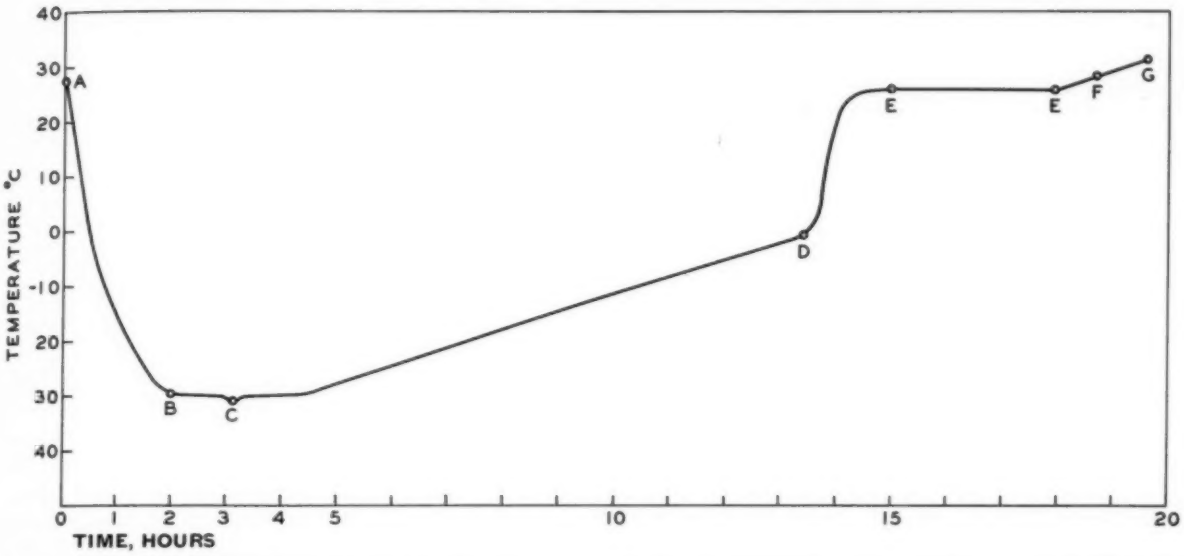
FREEZE DRYING UNITS

Radiant energy freeze drying units and conductance freeze drying chambers were considered for this paper. The former units utilize infra-red 10,000-35,000A° intensity radiation through glass product containers to heat the frozen solution during the drying cycle. Conductance freeze drying chambers are equipped with temperature controlled shelves which furnish heat by conduction during the drying cycle as well as facilitate the abstraction of heat during the freezing phase. Vacuum for this type processing is usually maintained at 50 to 100 microns. Most units are equipped with viewports for examination of the product during processing and with ultra-violet ray tubes to facilitate sterility. Such equipment is usually contained in sterile areas with humidity and temperature regulation. Recording instruments may be used to regulate processing cycles and to provide a permanent record of lot processed.

PRODUCT QUALITY

The quality of the pharmaceutical obtained by freeze drying is a prime consideration in product formulation. If it is assumed that such fundamental entities as chemical compatibility, percentage excess medicinal filled and product stability have been assured, the question of product appearance arises. The nature of the lyophilized residue with respect to color, homogeneity, and fragility determines to a large degree the consumer acceptance of the product. There are several factors of this nature to be considered concerning the lyophilized "plug." The term "plug" refers to a type of lyophilized product which is processed in its final market container. The aqueous solution is filled into a vial or ampul and frozen, then dried while the container is in an upright position.

FIG. I TYPICAL FREEZE - DRYING TEMPERATURE RECORDING



Legend, Figure I

The original recorded temperature (a) of the product to be frozen drops quickly when subjected to adequate refrigeration until it reaches temperature (b), the desired temperature for proper grain size of frozen plug. This temperature is maintained for a short interval to insure the proper grain size. Vacuum applied at this time may result in (c) a slight drop in temperature due to self freezing induced by the vaporization of any frost on outside of containers. Then follows a longer period of time denoting the sublimation of ice induced by high vacuum and the absorption of heat from the energy source. At the point (d) indicating the end of the initial phase of drying, a sudden rise in temperature is noted. At this point, the product begins the phase in which it is absorbing heat without the corresponding cooling caused by the sublimation of quantities of ice. The temperature rises rapidly and moisture is quickly driven from the product. Considerable care must be exercised as the product approaches room temperature or the final temperature of drying (e), so as to eliminate temperature deterioration. The drying curve must be leveled and held for several hours at this temperature (e), to insure complete dessication. The temperature is then raised several degrees (g), above room temperature (f), and vacuum broken in the chamber. This latter precaution eliminates the deposition of moisture as frost on and in the container when it is removed from the vacuum chamber. By utilizing this elevated temperature, dew point cannot be reached in the immediate vicinity of the container to produce moisture that may be easily absorbed by the now hygroscopic plug.

The volume occupied by the plug compared to its container capacity and the physical appearance of the lyophilized residue are factors of importance in merchandising these products. A small layer barely covering the bottom of a vial conveys the impression that the purchaser is getting little for his money. A plug which completely fills a container may cause difficulty in reconstitution with its diluent. A crumbly plug arouses suspicion as to the age of the product, and a discolored or bubbly plug may infer potency loss. Just how to obtain the proper plug size and appearance is often encountered as a problem in formulating lyophilized products.

THE PLUG

Examination and assay of some successful lyophilized products indicates that the percentage of solids in the frozen plug usually falls between seven and 25 per cent. This characteristic may be determined by weighing the dry contents of the vial and applying this determination to the volume occupied by the lyophilized residue. Pharmaceuticals with a percentage solid content in this range result in products with desirable plug characteristics depending on the nature of the medicinal ingredients.

Frequently formulas are difficult to lyophilize due to surface bubbling during the vacuum drying cycle and a crusty, heterogeneous mass results. Bubbling or foaming is often caused by freeze drying at temperatures above which there is eutectic separation.[16] In addition to temperature modulation, the eutectic point may be influenced by regulating the crystalline lattice separation. The use of higher percentages of solids resolves this difficulty. This may be accomplished by the addition of other medicinals, buffers and diluents as the substance which furnishes a primary crystalline network on which other materials may build to result in a solid plug of good appearance and ready solubility.

The inclusion of isotonicity influencing substances as sodium chloride or dextrose, which may be declared on the label without creating doubt with respect to potency or toxicity, is of assistance in raising the per-

(Continued on page 566)

by Milton A. Lesser

Keeping Pace with

Topically applied antihistaminic ointments, creams or lotions are valuable adjuncts in the therapy of various dermatologic conditions, especially pruritic dermatoses. Among itching skin disorders frequently benefited by the internal or external administration of these drugs are atopic dermatitis, contact dermatitis, pruritus ani and vulvae, generalized pruritus, and insect bites.[37] As remarked by Cohen,[61] topical application provides the direct, local action of the antihistamine and the protective covering action of the vehicle. The control of the pruritus minimizes the trauma of scratching and the secondary infection and thus promotes healing.

The advantage of using a topical preparation is well illustrated in the report of O'Rourke and Murnaghan[62] on the use of an antihistamine cream to alleviate mosquito bite reactions. Treatment of the bitten area with the cream was very effective; relieving the pruritus in over 80 per cent of the cases. The preparation was also effective in reducing the severity of the lesions. These results indicated that not only will individuals be subjectively relieved by the antihistamine cream, but also secondary infections that generally result from scratching will be considerably reduced.

However, there is growing evidence that there are limitations to the usefulness of topically applied antihistamines in dermatology. This was brought out in the replies to questionnaires received from 200 dermatologists by Ellis and Bundick.[63] The replies indicated that 94 per cent of the dermatologists had tried the topical use of the antihistamines, but that only 60 per cent still used them and less than 10 per cent prescribed them often. Those who had discontinued or restricted their use had done so because they believed this form of therapy was ineffective, tended to aggravate the dermatoses under treatment, or resulted in too high an incidence of contact-type sensitization.

In an editorial discussion[64] of this and other reports, it was noted that antihistamines vary in their skin-sensitizing power, but usually two to six per cent of cases become sensitized. It is advised that the doctor who thinks of using topical antihistamines should pay due regard to their sensitizing power, which is midway between that of the hazardous benzocaine derivatives and the old-fashioned oily calamine lotion.

It was largely on the basis of this sensitizing action and the risk of contact dermatitis that the Council on Pharmacy and Chemistry of the A.M.A.[65] decided to omit dermatologic preparations of antihistamine drugs from "New and Nonofficial Remedies." It will be recalled that the incidence of sensitivity reactions was responsible for similar action by the Council in the case of topical forms of the sulfa drugs and penicillin.

Pertinent in this connection is the statement by Phillips[66] that while cutaneous hypersensitivity to antihistamine creams undoubtedly exists, it should be stressed that in many cases the cream base and not the antihistamine content is the sensitizing factor. He is of the opinion that in cases where sensitivity to one antihistamine cream is discovered, a change to another, preceded by a simple patch test, is indicated, rather than abandoning a "very useful" form of therapy.

Also pertinent is the fact that among the dermatologists responding to Ellis and Bundick,[63] about one-fourth considered the local use of the antihistamines to be of value, being most useful in localized neurodermatitis and anogenital pruritus and of least value in moist areas.

Well worth noting are the conclusions reached by Cohen[61] in his unbiased attempt to evaluate the topical uses of the antihistamines. "In the final analysis,"

the ANTIHISTAMINES PART TWO

says he, "whether or not a particular physician utilizes topical antihistamine therapy will depend upon his own results derived from previous experience. With our present state of knowledge, the best method in clinical practice is to try the available drugs; since there is great individual variability it is suggested that these agents be tried in: anogenital pruritus (anus, vulva, scrotum); neurodermatoses; disseminated neurodermatitis (atopic eczema); eczematoid dermatitis; contact dermatitis (ivy, oak, sumac, occupational); lichen simplex; lichen urticatus; insect bites and stings; extraocular allergy associated and unassociated with hay fever." Cohen stresses that the antihistamines should not be applied to infected lesions nor to abraded or denuded areas. Medication should be stopped if such reactions as burning, redness or intensified itching occur.

Apparently the antihistamines are finding their appropriate place in dermatologic therapy. For this purpose they are provided as ointments, creams or lotions. In some of these preparations, the antihistamine may be the chief active ingredient or it may serve in conjunction with other components. A typical example of the former type of preparation, as given in the Florida Formulary,[66] is offered in the following antihistamine ointment:

Tripelennamine (Pyribenzamine) hydrochloride	0.6 Gm.
Washable ointment base, to make	30.0 Gm.

The washable base required in the above is made from:

Cetyl alcohol	9.2 Gm.
Stearyl alcohol	9.2 Gm.
Sodium lauryl sulfate	1.5 Gm.
Propylene glycol	10.0 Gm.
White petrolatum	30.0 Gm.
Water, distilled	100.0 cc.

An antihistamine cream given in this source is as follows:

Tripelennamine hydrochloride	0.60 Gm.
Glyceryl monostearate	4.50 Gm.
Cetyl alcohol	1.50 Gm.
Methyl cellulose	0.30 Gm.
Sorbitan monooleate (Span 80)	0.09 Gm.
Polyoxyethylene sorbitan monooleate (Tween 80)	0.09 Gm.
Water, distilled, to make	30.00 Gm.

Another preparation, this one of British origin,[67] calls for the use of:

Antazoline (Antistine) hydrochloride	2.0 Gm.
Polyethylene glycol 600 monostearate	5.0 Gm.
Cetyl alcohol	14.0 Gm.
Liquid paraffin	10.0 Gm.
Soft paraffin	7.0 Gm.
Water and preservative, to make	100.0 Gm.

Calamine lotions containing antihistamines have become quite popular during recent years. A formula for such a lotion, based on calamine lotion USP XIV, has been given[64] as follows:

Pyrilamine maleate	150.0 Gm.
Calamine	800.0 Gm.
Zinc oxide	800.0 Gm.
Polyethylene glycol 400	800.0 cc.
Polyethylene glycol 400 monostearate	200.0 Gm.
Water	9,000.0 cc.

Heat the polyethylene glycol 400 monostearate to 70° C. on a water bath. Dissolve the pyrilamine in all of the water heated almost to boiling, and add at once to the monostearate. Stir until the temperature drops to 40° C. Mix the zinc oxide and the calamine and make into a paste with polyethylene glycol 400. Gradually add the cooled monostearate emulsion and continue stirring until a uniform suspension is formed.

Another preparation (Histar) which is available for the treatment of dermatologic conditions consists of a combination of crude coal-tar extract and an antihistamine incorporated in an emulsified hydrophylic base. In tests made by the Friedlaenders,[68] this ointment was used in the local therapy of 67 patients with chronic eczematous and papulo-squamous dermatoses. The symptomatic response in 44 cases was considered excellent. In nine others a fair response was obtained. Of these patients, 11 showed no benefit. Only three patients in this series failed to tolerate the combination. Each was found to be sensitive to the tar component, and were able to tolerate the antihistamine and base without difficulty.

Zirconium oxide-antihistamine combinations in ointment or cream bases have proved effective in the prevention and treatment of rhus dermatitis (e.g. poison ivy, oak and sumac).[69,70] Barrett[71] found that such a cream is effective in relieving the pruritus of rhus der-

matitis in 24 hours and that it is also effective on lesions existing from a few hours to several days. The same preparation, applied to the hands, forearms, face and neck of men being exposed to rhus diversiloba under actual field conditions, reduced the incidence of poison oak dermatitis from 21.1 to 9.6 per cent.[72]

A novel use for antihistamines is in the formulation of anti-irritant lipstick. According to the patent[73] describing such use, it has been discovered that if an antihistamine is added to an indelible lipstick base, the irritative effect of bromofluorescein is reduced and even eliminated.

The more recent literature provides further data on the fungistatic properties of the antihistamines. Several *in vitro* studies[74,75,76] have served to verify the antifungal action of a number of these agents. From the studies made by Landis and Krop,[77] the effect of the antihistamines is due to their interference with the histamine metabolism of the fungi. Clinically, Spoor and Yang[78] obtained good results in the treatment of athlete's foot with an antihistaminic preparation.

It has been pointed out[3] that the local anesthetic effect of the antihistamines is also useful in relieving the pruritus that usually accompanies fungus infection. Indeed it is now well established that the benefits in dermatologic conditions of topically applied antihistamines is often due to a large extent to this local anesthetic action.[2,61,79]

This local anesthetic effect has found valuable application in other phases of medicine. In considering the role of these substances as anesthetic agents in broncoscopy, Kleitsch[80] remarked that if it is possible to use an antihistamine for topical anesthesia, then the side effects of smooth muscle relaxation, secretory inhibition, analgesia, and prolongation of the refractory phase of muscle, instead of being complicating effects are indeed desirable. His own studies confirmed these views. He found that the topical anesthesia produced by a mixture of an antihistamine (Tripelennamine) and tetracaine is profound and requires no premedication. On the basis of such observations, Kleitsch felt that he could recommend this solution as a superior topical anesthetic in peroral edoscopy.

As noted by Cohen,[61] a number of investigators have found that antihistamines are safe and effective for producing local anesthesia in gastroscopy. Fitzpatrick and his associates[81] have employed antihistamines as local anesthetic agents for urethral manipulation. They used the drug in solution, ointment and pellet forms and found these preparations particularly useful for patients who show sensitivity to the usual topical anesthetic drugs.

Other applications for the topical anesthetic action of antihistamines are cited by Stubbart.[82] He has observed that the anesthesia afforded by these drugs aids in the passage of gastric tubes in apprehensive patients. The discomfort associated with the prolonged use of these transnasal catheters can also be greatly relieved by applying a spray of an antihistaminic solution. Patients unable to eat because of the pain and discomfort of tonsillitis, stomatitis and tonsillectomy were able to take food with relative ease shortly after gargling with an antihistamine solution. By placing a small amount of the powdered drug in the cavity, it was possible to alleviate the pain experienced after dental extractions and, in some cases, due to carious teeth.

He also reported that in proctology, ointments and solutions of antihistamines were effective for relieving painful hemorrhoids. Cotton wicks, wet with an aqueous solution of the agent, were used with complete satisfaction in the postoperative period following hemorrhoidectomy. The wick method has also been used to provide prolonged relief in cases of otitis externa. By filling the external auditory canal with a solution of an antihistamine, sufficient anesthesia is obtained in a few minutes to permit cleaning and examination in most cases.

Stubbart states that sterile solutions, of 0.5 to 1.0 per cent concentration, provide adequate anesthesia when injected in a routine infiltration technic to permit minor surgery. He reports that no undesirable side-effects were observed.

Apparently, says he, the use of antihistamines in premedication is satisfactory. However, their use to produce general intravenous anesthesia has been accompanied by respiratory difficulty.

In this connection it should be noted that antihistamines are capable of potentiating or improving the action of various anesthetics and analgesics. For example, the investigations of Lightstone and Nelson[83] indicate that the common antihistamine drugs significantly prolong the sleeping time of pentobarbital anesthesia in the rat. Liver analysis also indicated that the antihistamines do not seem to interfere with the detoxication of the pentobarbital. In the opinion of the investigators, the mechanism by which the antihistamines prolong the sleeping time of the barbiturate is apparently unrelated to their common side actions.

Of related interest are the clinical studies on improvements in obstetric analgesia reported by Cappe and Pallin.[84] They observed a high degree of durable pain relief in patients who received intravenous infusions of five per cent alcohol in five per cent dextrose in water combined with fractional injections of an antihistamine (e.g. diphenhydramine hydrochloride).

The last few years has seen further affirmation of the value of antihistamines in the prevention and treatment of motion sickness.[85] For example, Chinn and his associates[86] reported that good protection against motion sickness during training flights was obtained with a mixture of the antihistamine, diphenhydramine hydrochloride, and hyoscine hydrobromide. Such a combination is now available commercially in tablet form.

The symptoms of nausea and vomiting, so prominent in motion sickness, are frequently alleviated by the antihistamines when these discomforts are present in other disorders. Lash[87] has added to the data which show the value of antihistamines in the treatment of

(Continued on page 569)

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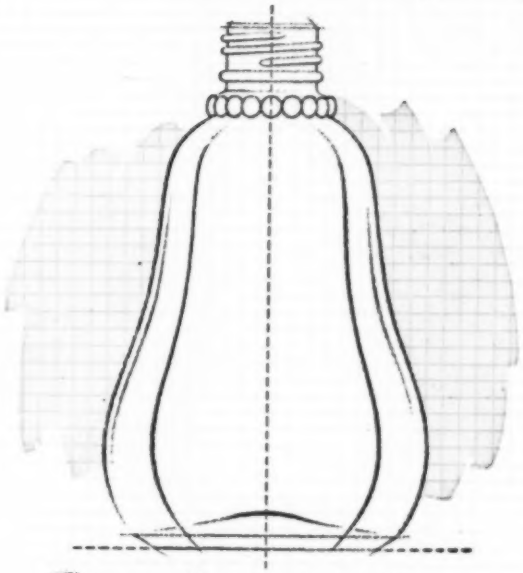

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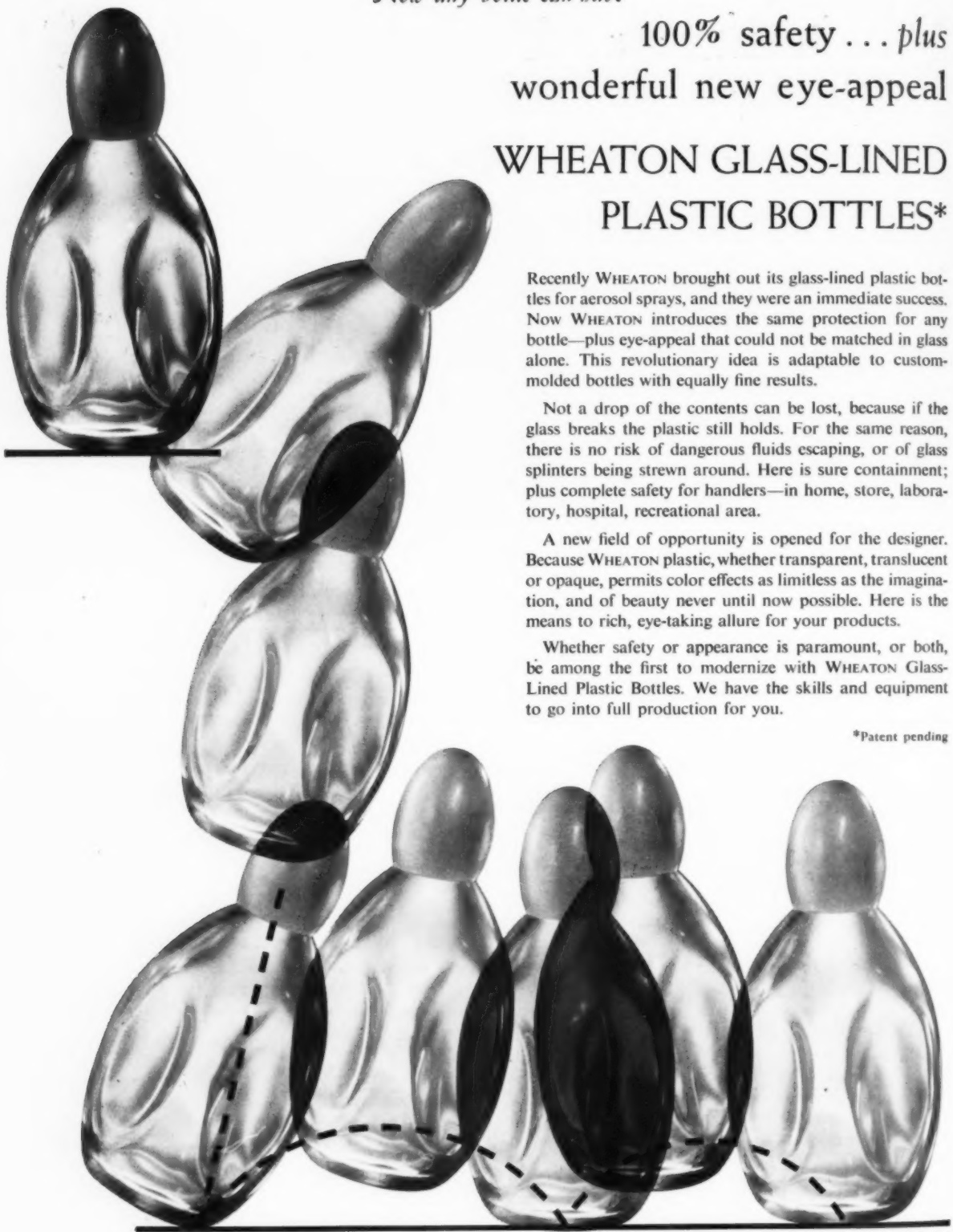

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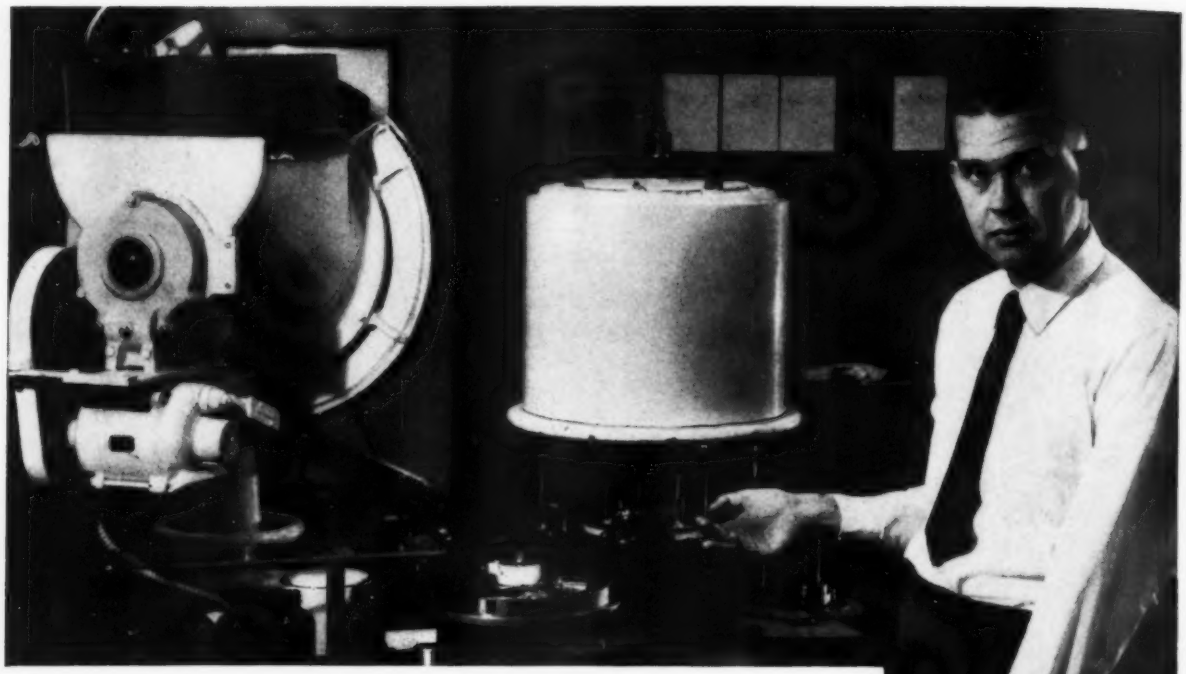

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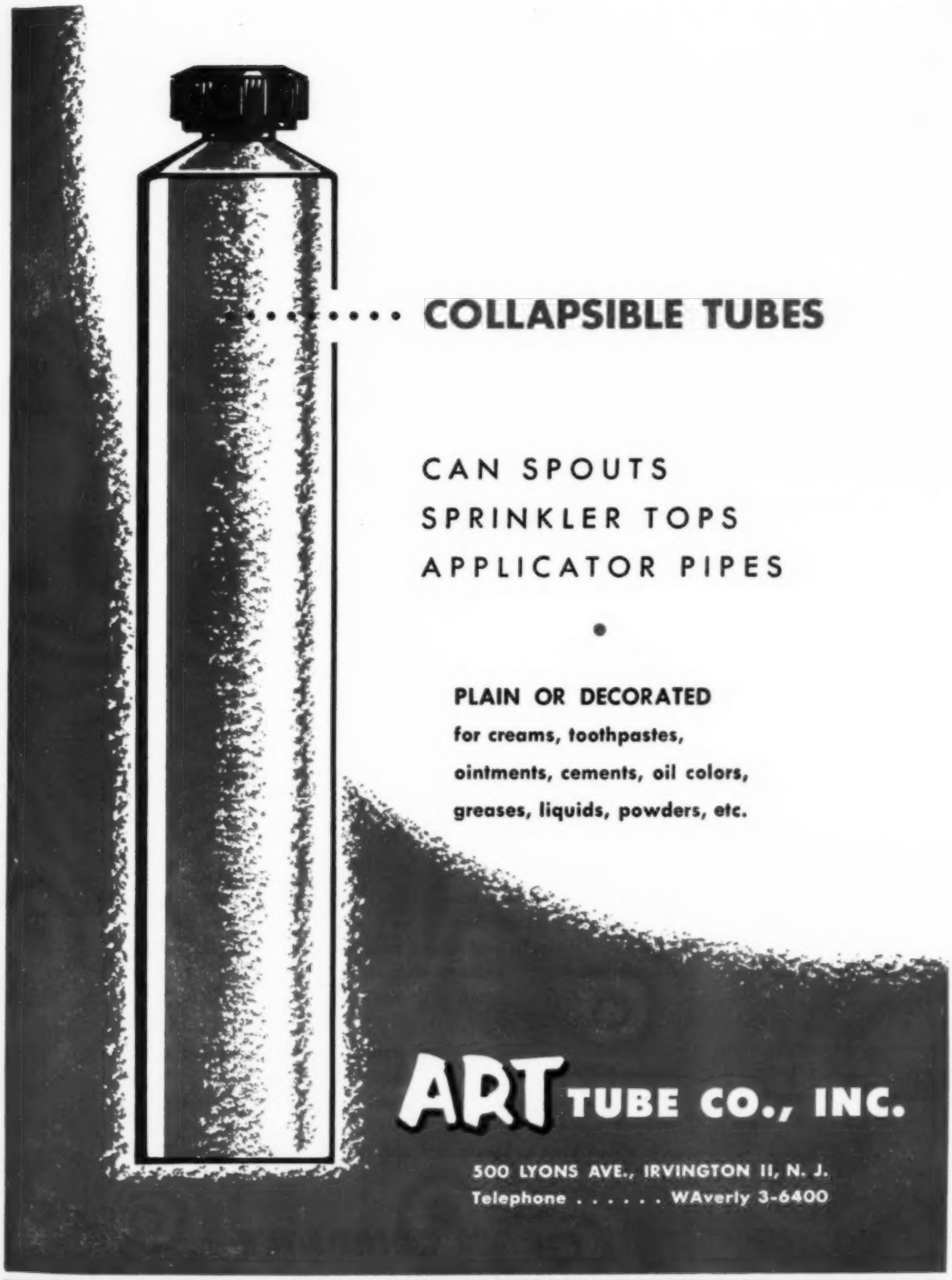
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TAILOR-MADE PACKAGE SERVICE

PILLS in BAGS

Capsules or tablets are automatically counted into bottles, 100 capsules or tablets to each bottle.

Lederle Laboratories has instituted the packaging of capsules and tablets in polyethylene film for bulk shipment and storage at its Pearl River, N. Y., plant. The new packaging method is termed the Century-Pak, each of which consists of 100 capsules or tablets placed in a polyethylene bag, four inches by six inches, or four inches by four inches, and heat sealed at the opening. A number of these bags are then placed in drums for bulk shipment.

Each bag is clearly labeled to identify its contents. The type of polyethylene film is one that is specially treated so that ink will permanently adhere to it.

(Continued on page 479)

The contents of the bottles are then manually transferred into individual polyethylene bags. Each VISQUEEN bag, with 100 tablets or capsules, is a Century-Pak.

Each bag then is placed into a mechanical sealer which heat seals the opening.

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Du Pont CEL-O-SEAL bands
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protect contents, establish family identification

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Impression-making Du Pont "Cel-O-Seal" bands will work for your package, too! They hold closures tight, guard against tampering and spillage, inspire consumer confidence. And "Cel-O-Seal" bands are available in a wide range of colors . . . can be printed with an eye-catching sales message or slogan.

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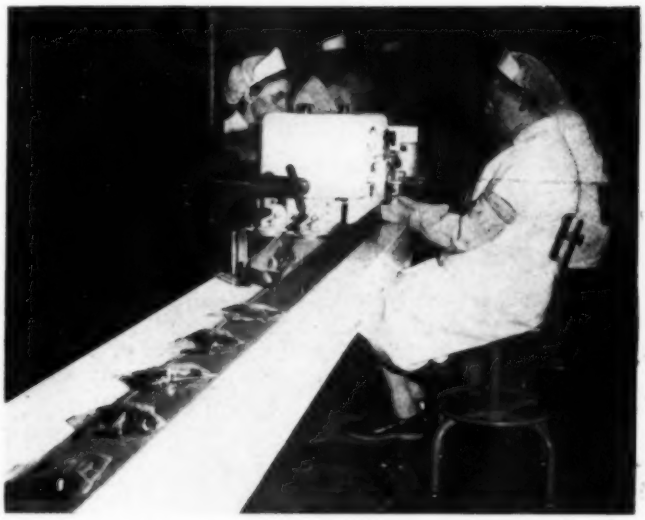
. . . THROUGH CHEMISTRY

PILLS in BAGS (*continued*)

In the filling process, capsules or tablets are automatically counted into bottles, 100 to each bottle. Then the contents of a bottle are transferred by hand to a polyethylene film container. The containers are then heat-sealed, and then packaged in their final container—a canister.

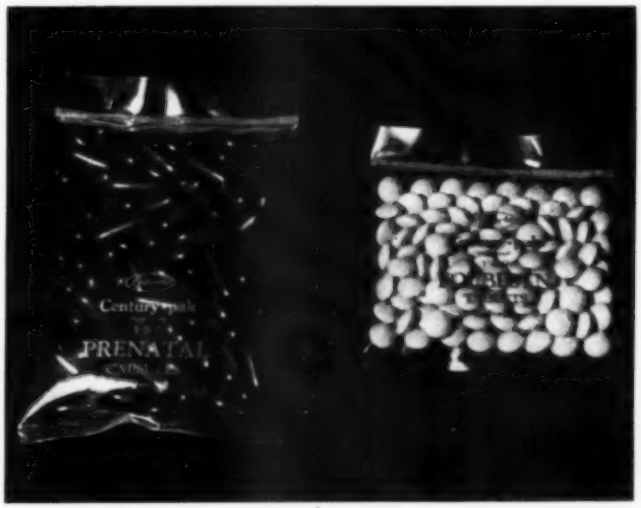
This method of packing is said to offer advantages to Lederle and to the retail druggist. Advantages claimed are that it protects the products against moisture, reduces chipping and breaking, and helps prevent malformation and sticking of capsules to the bottom of the drum even after long periods of time.



After sealing, the Century-Paks move along a conveyor belt for final packing

Here, the bags are manually placed into wall insulated and sealed cardboard canisters for shipment. Normally, 50 Century-Paks are placed in each canister; however, for greater bulk shipment several of the faster selling products are packed into a larger container holding 250 Century-Paks—25,000 capsules.

Two typical Century-Paks. Note that the contents are clearly imprinted on the polyethylene bags.



PHOTOS COURTESY OF VISKING CORPORATION PLASTICS DIVISION, TERRE HAUTE, INDIANA

Packaging and Selling

Not so Soft in Super-Markets

According to an article in the Journal of Retailing, a high of 50 per cent of all supermarkets now carry soft goods.

Gordon B. Cross, in an article in this Journal, analyzes some of the problems which supermarkets are encountering when they stock soft goods. Most of these problems are emphasized and exaggerated in the products of our trade and are much more serious than in most other fields of soft goods selling, from the supermarket's viewpoint.

MARKDOWNS

The high markup on soft goods has been the chief lure persuading the supermarket into these fields. Very often, these high markups look much less attractive after losses from depreciation are considered. In cosmetics, fashion, color, obsolescence because of chemical discoveries and particularly the very high mortality of many products in this dynamically changing field, make markdowns a very serious problem for a supermarket which hopes to establish a cosmetic and toiletries department, rather than to just high-spot a few dominant brands.

MERCHANDISE ASSORTMENTS

The modern supermarket carries approximately 4,000 items. Branded food products are mostly single specialties, not many full line brands. In cosmetics, one single item such as lipstick, for instance, will necessitate many different items to give the full range of shades and styles and fashions which keep the sale of these products at a high peak.

TURNOVER

Soft goods turnover is almost universally much lower than food products. The mixing of high turnover and low turnover products on the same floor space creates a number of merchandising problems.

PACKAGING

In many cases packaging of soft goods is not adapted to self-service, from the viewpoint of handling and soiling.

It can't be denied that a great many supermarkets, particularly on the Coast and in the Southwest, have made conspicuous success in merchandising a wide variety of soft goods products, including several fields of apparel, the products of this industry, candy and other goods.

As competition intensifies, however, in food retailing, soft goods merchandising problems which have not received real attention up to now may emerge in a way that would change this present rosy soft goods picture in the supermarket.

PILFERAGE

This is one of the really serious problems in soft goods selling in the supermarket.

Wholesale Facts

"Facts on 1953 operations for Service Wholesale Druggists" has just been published by the National Wholesale Druggists Association. This is an analysis of wholesale operating costs containing many valuable facts.

Directory

The First Pocket Edition of the American Druggist's Directory of drug markets provides in a handy size the complete facts on drugstore distribution in America. This new directory is organized by cities which makes it very convenient for the salesman or the sales manager to spot the chains, the wholesalers, the sales agents, the department stores with prescription departments, the pharmacy colleges, associations pharmacy particulars, daily newspapers, radio and TV stations, all with the names of people to be seen.

Creative Thinking

L. Bamberger & Co., a leading department store, awarded a gold medal to its cosmetic buyer for persuading a manufacturer to develop the "Pixie" line of cosmetics for teen-agers. This looks to us like the kind of creative thinking over and beyond the call of duty that deserves a gold medal.

Growing Impulse

There are indications that self-service selling and open display are increasing the amount of retail purchases based on "impulse." In other words, the convenience of self-service and the wide range of clearly visible products to act as a reminder to the woman shopper is tending to reduce or eliminate the necessity on her part for a carefully prepared shopping list prior to the visit to the store.

NEW! Colorful Plastainer Vials BY OWENS-ILLINOIS

Plastainer vials are now available in a wide variety of attractive colors, opaque and transparent, with colorful matching closures. They are typical examples of the many sizes, shapes and colors of containers the broad plastic molding facilities of Owens-Illinois make possible to fill your needs.

You can package anything from candy beads to fishing tackle in Plastainer vials by Owens-Illinois. They protect contents from handling, air and moisture until used. Plastainer vials won't split or crack . . . have wide diameter for easy filling and stable base . . . come in 6 sizes: 3 to 15 drams.

Owens-Illinois packaging know-how and high-quality standards offer you the finest in plastic molding facilities . . . Injection molding . . . Compression molding . . . A complete range in plastics for packaging, for specialties.

Branch Offices:

Albany ..... New York	Columbus ..... Ohio	Memphis ..... Tennessee	Pittsburgh ..... Pennsylvania
Atlanta ..... Georgia	Dallas ..... Texas	Milwaukee ..... Wisconsin	Portland ..... Oregon
Baltimore ..... Maryland	Denver ..... Colorado	Nashville ..... Tennessee	Richmond ..... Virginia
Birmingham ..... Alabama	Detroit ..... Michigan	New Orleans ..... Louisiana	Rochester ..... New York
Boston ..... Massachusetts	Fresno ..... California	New York ..... New York	St. Louis ..... Missouri
Buffalo ..... New York	Houston ..... Texas	Oakland ..... California	St. Paul ..... Minnesota
Charleston ..... West Virginia	Indianapolis ..... Indiana	Oklahoma City ..... Oklahoma	Salt Lake City ..... Utah
Charlotte ..... North Carolina	Jacksonville ..... Florida	Omaha ..... Nebraska	San Francisco ..... California
Chicago ..... Illinois	Kansas City ..... Missouri	Peoria ..... Illinois	Seattle ..... Washington
Cincinnati ..... Ohio	Los Angeles ..... California	Philadelphia ..... Pennsylvania	Toledo ..... Ohio
Cleveland ..... Ohio	Louisville ..... Kentucky		

OWENS-ILLINOIS PLASTICS
AN (O) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES • TOLEDO 1, OHIO

NEW...

A refillable metal compact for cake powder!

New Idea:
Powder Pan Retainer

SCOVILL HAS DESIGNED a metal compact for compressed (cake-type) powder that can be refilled when empty!

There has long been a crying need for this type of compact which combines all the fine features and attractive appearance that can be obtained only in a fine metal container.

This new "gold vanity" has a powder pan retainer that is an integral part of the compact. It is held securely in the compact, yet snaps open easily when it is time for a refill. (This will increase your refill business.)

The refillable compact is available in a variety of square and round shapes, can be finished to any specifications, and may be lettered or decorated as desired.

Ask a Scovill representative to show you this latest new product developed by Scovill's Drug and Cosmetic Container Division. Maybe it's the answer to a problem you're facing right now!

At any rate, please remember this. Call us *any* time you have a container problem. We are *sure* that our engineers will be able to help you as they have others.

SCOVILL-MADE Containers

A product of SCOVILL

SCOVILL MFG. COMPANY, WATERBURY 20, CONN.

In a recent survey by du Pont seven out of ten buying decisions are made after the woman shopper enters the store. These women do not use a shopping list and devote only a little more than a minute of her time in buying each item.

The seven out of ten buying decisions reported in this recent survey are an increase over the two out of three impulse buying decisions shown by a du Pont survey of 1949. The average "impulse" buying rate for all foods is found to be 48 per cent of this survey compared with 38-40 per cent in a previous one.

The widely accepted vital importance of the impulse purchase for all kinds of merchandise which receive visible display emphasizes the growing importance of packaging and of a point of sale strategy as well as consumer advertising. Modern marketing in the retail store is no longer a one-way street but at the very least three parallel and equally important avenues.

A New Industry?

"Sucrochemistry" is a word we may be hearing a great deal more about in the future. As a starting point, sucrochemistry is reported to have developed a new detergent made from sugar which is "effective, mild and inexpensive."

In this wonderful age of chemistry and research, almost any basic organic material may be the foundation of a great new industry. We are in the middle of ushering in a great new section of the chemical industry "petrochemicals." Now it seems that sucrochemicals are at the threshold.

Do Sales Meetings Waste Money?

According to Edward H. Weiss, the President of Weiss & Geller, Inc., an advertising agency, in a recent speech, this is very often the case.

According to Mr. Weiss, within the next year, more than $419,000,000.00 will be spent on sales meetings.

Here are a few quotes from this speech:

"Management's failure to understand the real feelings and emotions of its salesmen is the trigger which sets off a chain reaction whose end result, unhappily, is that salesmen often return to their territories after a sales meeting either confused and bewildered, angry and rebellious or possibly worse, apathetic and disinterested."

"Because salesmen feel this lack of understanding on management's part, they frequently come to a sales meeting wearily wondering in what guise the same old stew is going to be served to them this time."

"Salesmen are not participants in such meetings—they are victims."

"The salesman is by nature a rugged individualist. That is why he is a salesman in the first place. Our first studies have shown that at most sales meetings, he is actually reminded that he is a schoolchild, helplessly listening to teacher threaten him; exhort him to increased effort, or humiliate him."

"Management will be able to end this costly salesmen's strike when it understands that salesmen resent being treated like children; that they resent being talked down. to, that they must be allowed to participate instead of merely being allowed to observe."

Coming Age of Vending

Vending machines now retail more than 1.5 billion dollars a year. The products sold through vending machines are still limited in number despite many new and unique applications in the last few years. The fact that 1½-billion-dollar sales can be made primarily in tobacco products, candies and soft drinks is one indication of the colossal potentiality of this method of retailing.

We like to think of self-service as a great marketing invention of this era and the last word in retailing. We forget that the vending machine has several startling social and economic advantages over the self-service grocery store.

In the self-service grocery store the customer has to go to the store. This means finding a convenient time. It means travel and it means extra work. On the other hand, the vending machine is more and more going to the customer. Locations of vending machines are selecting high traffic points where the customer has to be anyway for some other reason or such places as large factories, large apartment houses, etc.

In spite of the fact that a high percentage of the shoppers in a grocery store are employed and have little time for shopping and in consequence have to build up a big traffic bottleneck of delays and frustrations on two evenings a week and on Saturday, labor problems have prevented retailers from giving complete time-convenience for shopping. The vending machine in a factory or an apartment house or some other traffic center operates without additional cost around the clock.

Self-service still means standing on line at a counter to have the products checked and to pay and make change. There is no standing in line usually for the vending machine and the change mechanism is one of engineering's modern miracles.

We have long felt that the grocery super-market which has so excited this industry, as a wonderful new method of distribution for low priced, pre-sold necessities may be only a transitory passing period for this industry's distribution. For products like tooth paste, shaving cream, aspirin, etc., that is, the every day staple necessities of our industry, we don't really need a super market. What we need is the utmost convenience and accessibility in making such products available to the customer.

Drug Store Survey

The Neilsen report on retail drug and proprietary store sales in 1953, just issued, is a valuable analysis which should be studied by every manufacturer selling to retail drugstores.

In addition to basic economy factors which have affected the growth and sales of drugstores, this analysis includes a study of retail drugstore sales by territorial divisions, sales by independents and chains and a study of drug items in food stores.

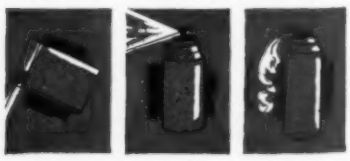
It has always puzzled us as to why there has been no growth in the number of drugstores during the past decade when everything else in America has multiplied so substantially. According to this survey, the number of drug and medicine stores in 1948 totaled 56,000. This totalled seven per cent of chain drugstores and

Can we spray an idea your way? Package for aerosol dispensing . . . and do it in glass like our sales-minded client, Bourjois, does. In this suave push-button bottle lies the essence of sound merchandising. Push-button containers invite immediate attention and examination . . . give both men and women shoppers cleanliness, protection, economy. Glass aerosols assure universal sales appeal for personal products like perfumes, sun tan oil, hair dressings, deodorants, etc. . . . through high content visibility, color display, and an unlimited range of inexpensive bottle shapes and sizes for flexible, competitive pricing. Capitalize on the trend to glass aerosols now. Boost profits. Contact us for a free product evaluation.

Perfume: Bourjois
Bottle: Maryland Glass
Valve and gold cap: Risdon
Gold foil label: Foxon
Filled by CONTINENTAL

COMPLETE FILLING SERVICE. Get Continental's famous "follow-through" on liquid, spray and foam packaging . . . in glass or cans. Two modern Midwest plants give you on-time delivery and freight savings plus warehousing and drop-shipping in bulk lots. We handle paper work, and protect your product with lab analysis *before* . . . quality control *during* . . . and careful handling *after* production.

CONTRACT AND CUSTOM FILLING



LIQUID *SPRAY* *FOAM*

MAIN OFFICE • 123 NORTH HAZEL STREET, DANVILLE, ILLINOIS

CONTINENTAL FILLING CORPORATION

PLANTS • DANVILLE, ILLINOIS — HOBART, INDIANA

the remainder of independent drug and proprietary outlets. According to the survey, "From recent estimates there is no indication that the number of drug and proprietary stores in existence during the current year of 1953 differed appreciably from the number of units in operation during 1948." Drugstore sales in 1953 amounted to 4.8 million dollars or 800 million more than 1948. We certainly would like to know the answer to this phenomenon of lack of growth in the number of drug stores.

Groaning Selling Costs

There is a trend among the dominant national advertisers in the soap and food field to pay grocery retailers a fixed sum for handling coupons on promotion. One leading advertiser who has been deluging the grocery trade with coupons and promotions has decided to stem the tide of retail revolt at all these additional handling charges by allowing 2½ cents each for handling coupons in promotions.

There is no question but that the retailer, in this one particular instance, is entitled to this payment for this extra work involved. If these coupons and promotions all contributed to expanding business in the retail store, there would be no excuse for this payment because it would be legitimately part of the retailer's contribution to expanding sales. But it is becoming more and more evident, in this period of frantic promotions, that a large part of the sales created by the promotion is not increasing consumption of the kind of products promoted, but is merely taking the sale, which a retailer would get anyway, away from a competing manufacturer.

Business has not as yet publicly and properly appraised the disgraceful record of marketing men as compared to production men during the last generation. This is a subject of research and discussion that should be at the top of the agenda in our rapidly growing business administration schools in universities. There must be a limit to what consumers will absorb in extravagantly high competitive selling costs which add nothing which we can perceive to the economy. This particular industry, selling ethical drugs and cosmetics, is among the conspicuous leaders in reckless extravagance in distribution costs. Recent financial statements of some of the ethical drug manufacturers show expanding sales but with these expanding sales show such high costs and increase in selling that there is a decline in profits. The twin sales forces of the retail salesman and the detail man plus advertising and direct mail are piling a frightful burden of selling costs on this industry which is reflected in the final price the consumer pays for medicine and which constitutes a field of vulnerable criticism which may some day harrass this industry.

In the cosmetic business, the extravagant excesses in some forms of selling are an indictment of American business efficiency which exceeds anything we can complain about in European production methods. Some cosmetic manufacturers, in addition to the regular 40 per cent discount to retailers, are also paying to the retailer the full salary of a retail sales clerk; a 10 per cent PM as an alternative; all or part of the retailer's local advertising on the manufacturer's particular product; payments for space in the retailer's catalogue and direct mail costs; a percentage of window and in-store display costs and sometimes a rental of counter space. This is not to mention payments for retail recreation and entertainment and for all we know, from what we occasionally hear, putting the retailer's children through college.

It is interesting to observe that the greatest extravagances in distribution costs are very largely in the fields where national advertising predominates. In other words, the very section of our economy where the primary function of advertising is to reduce the cost to the consumer, is the very place where we find this conglomeration of high and questionable selling costs.

An observer can hardly help but reflect that the growing and flourishing discount house is simply a symptom of and a protest of reckless extravagance in distribution cost.

Super-Markets Make Good Locations

Apparently it is a good idea for a retailer to locate near a super-market. A few months ago, in this department, we stated that if we were running a drug store we would like nothing better than to be located right next door to the most successful super-market possible. Now the Family Circle Magazine has employed James M. Vickery Company to interview and research customers in non-food stores in three neighboring shopping centers. Vickery found that as much as 70 per cent of the customers interviewed in non-food shops also shopped in the super-market and that 40 per cent of them were planning to shop at the super-market on the same trip.

Big Country Market

According to Household Magazine, five out of nine of retail drugstores are located in places having less than 50,000 population. This part of the United States accounts for 65 per cent of the population and 63 per cent of all U. S. families. Also in places of less than 50,000, there are 26,912,837 children below fourteen years of age compared with 11,430,490 children living elsewhere.

Package Does Count in Success

Most new products fail to make the grade in the competitive struggle for customer recognition. There have been a number of surveys showing this in the past and we have pointed out many times that the cosmetic industry probably leads all industries in the number of new products launched that fail to obtain a successful life of over five years.

Hilton & Riggio, an advertising agency, in a survey of 200 manufacturers, found that only 19 per cent of new products reaching the American market-place made the grade as successful selling items.

These products in 77 per cent of the cases, cost the manufacturer more than expected and in 70 per cent of the cases, took longer than expected to become established.

According to this agency, packaging was found in the survey to play a relatively unimportant role.

The agency should certainly have surrounded with qualifications the statement that packaging has played an unimportant role in the successful launching of a new

Our finest quality glass stoppered bottles for perfume and toilet water

Tester Bottles

Left: No. H-900 (footed)
No. S-7222 elongated stopper

Right: No. H-900
No. S-300 elongated stopper

No. 352

Available in 7 sizes from ⅛ oz. to 8 oz. Supplied plain or with fired-on ceramic labels.

No. 435

Made in 3 sizes only—½ oz., 1 oz., ¼ oz. Available plain or decorated.

CARR-LOWREY GLASS CO.

Designers and manufacturers of fine glass containers

Factory and Main Office: BALTIMORE 3, MD. • *New York Office:* 40 W. FORTIETH ST. • *Chicago Office:* 1572 MERCHANDISE MART

product. Too many factors enter into this kind of a situation to let a loose statement of this sort hanging in the air. For instance, it is unquestionably true that there is a huge variation in the place a package can play in bringing and maintaining success for a product. There is a whale of a lot of difference, for instance, between the Stoppette package or the Sportsman, Shulton and many other packages and the packaging of some hardware item.

It would be a very interesting study to determine just how much relative importance the package plays in obtaining and holding a successful position for different kinds of products in different industries.

Shifting Security

"The security of a business shifts from capacity to produce the ability to sell." That is the history of every successful business as it gets bigger and bigger." The quote is from A. J. Gallager, business and market analyst, from an article in Printers Ink recently.

Stormy Lipstick Markets

In this department in the June issue, we had an article headed, "Stormy Weather for Lipsticks."

This article commented on the entry of Toni into the lipstick market with a new lipstick and with an advertising appropriation stated to amount to several million dollars. At the same time, it was reported that Lanolin Plus is bringing out a new lipstick and that the present factors in the lipstick industry, that is, such companies as Revlon, Hazel Bishop, Max Factor, Hudnut, Coty and others were revving up advertising and promotion plans to meet this new competition.

So far as marketing to women goes, lipsticks are one of the most universally used of all the packaged branded products. It is agreed generally throughout the industry that there is no potential for market expansion in lipsticks except with the normal growth of population. Therefore, the entry of Toni with an advertising appropriation which will require the sale of at least ten million dollars in lipsticks to maintain that appropriation means one of the greatest "shouldering out of way" in advertising history must be accomplished for Toni to gain a toe hold in the lipstick market.

Toni's entry into this super-competitive and completely saturated cosmetic market is all the more remarkable in that Toni has a conventional package has certainly so far not said anything new about their lipstick to warrant even a trial period, and is dressing up old cliches such as the overdone color pitch to justify their entry into this particular field.

With the new suit against Gillette by Hazel Bishop, Inc., the lipstick pot begins to boil with renewed activity. Hazel Bishop claims that Toni decided to enter the lipstick trade and to compete with Bishop and "wrongfully and unlawfully plotted, planned, and conspired fraudulently to acquire full knowledge of (a) all aspects of the plaintiff's business in the lipstick trade; (b) plaintiff's methods and channels of distribution; (c) plaintiff's methods of merchandising and promotion; (d) plaintiff's advertising format, copy and phraseology; (e) plaintiff's future product development and promotion plans; (f) plaintiff's secret and confidential market and consumer studies and information and (g) each and every element of and factor contributing to plaintiff's said goodwill and reputation."

The untutored layman would conclude from reading these complaints that Toni was a blushing debutante in cosmetic merchandising and that Hazel Bishop had pioneered in developing a lot of secret methods in promotions, in market studies and in advertising and that they had developed a secret and hitherto unknown type of retailer to serve as a channel of distribution for lipsticks.

Nevertheless, since this hot war in the lipstick industry has to generate a number of bloody battles, the complaints whether offered with a tongue in the cheek or not, do serve as a basis of conducting the fight on at least two fronts. That is in the courts as well as in the market place.

Hazel Bishop claims that Viv, the Toni lipstick "simulates, imitates and copies" the Hazel Bishop lipstick by duplicating its appearance, packaging, its channels and methods of distribution of sales and also its promotional and advertising ideas, its copy, its form and its phraseology.

Hazel Bishop claims that it is now the largest selling lipstick with the sale of more than fifty million lipsticks since 1949, with estimates that it will sell 22 million lipsticks in the fiscal year ending October 31. Hazel Bishop also estimates that it will do fourteen million dollars in sales during this fiscal year of which approximately ten million will be lipstick sales and that the company will spend $4,500,000 in advertising.

Among the concepts which Hazel Bishop claims are either unique or exclusive with its operations are: (1) "Two-way lipstick." (Conventional or non-smear.) (2) A "lasting," "long lasting" or "longer lasting lipstick" which remains vivid even after blotting. (3) Selling lipsticks at prices of $1.10 and 59c. (4) Affixing an assortment of lipsticks to a display card or case. (5) Shipping cartons which can be opened up into display trays. (6) The use of a "golden colored cylindrical metal case with a dome shaped cap."

These conspicuous achievements claimed by Hazel Bishop will undoubtedly be made by the defense with equally interesting and positive testimony.

Package Requirements

Jim Nash, New York designer, had some pertinent remarks to make about the newly-designed package of Bakers Cocoa.

"The face of this package is as effective as any point of sale poster in achieving sales for the grocer. Its clean quality appearance not only attracts but holds the eye. But the other three sides of the package are important in stimulating repeat sales when the package is in the kitchen. On the new Bakers Cocoa package the sides and backs incorporate principles that I consider potent sales builders."

Speaking of using the front of the package for product identification and point of sale display, the other three sides of the package for product description and product use and the top and bottom of the package for identification if it should be laid flat on the shelf, reminds us that we have heard no solution as yet to a still more complicated problem for packages.

MANY Styles AND Sizes

...THERE'S AN ANCHOR CAP FOR EVERY SEALING PURPOSE

ANCHOR HOCKING makes eight stlyes of metal and molded, screw and lug caps for medicinal and health products, toiletries, cosmetics and household chemicals. Each is designed for specific sealing purposes—all provide dependable, economical, attractive and efficient seals.

The uniformly high quality of Anchor Caps is the result of practical research and engineering, careful selection, testing and control of raw materials, high manufacturing standards and thorough quality control through laboratory tests and regular inspections.

If you package or contemplate packaging in glass let us recommend and send samples of the closures best suited to your particular needs. The services of our Package Engineering and Research Laboratories are also available to help you solve glass packaging problems.

Anchor Amerseal® Caps are available in 18 sizes—20 to 120 mm., lacquered, coated or privately decorated. Cap offers ultimate in convenience for consumer in removal and reseal. A simple quarter-turn and it's off—a reverse quarter-turn and it's on again.

ANCHOR HOCKING

GLASS CORPORATION
LANCASTER, OHIO
★
The Most Famous Name in Glass

Package Doin's . . .

Package Competition

The Package Designers Council, a non-profit organization made up of the country's leading package and industrial designers has announced its annual competition for the best package designs of 1954. The Council will also present the Irwin D. Wolf Award for the best American Package or packaging award.

Entries for all American-designed packages must be in the possession of the Committee by November 22 and should be mailed to Package Designers Council, 66 West 38th St., New York. These must be accompanied by an official entry blank securable through Council headquarters.

All entrats must submit an actual three-dimensional package, with or without contents, currently in mass distribution. Only those packages which have been on the market since October, 1953, will be accepted.

Perfume Atomizer

Parfums Corday now has a new aerosol Perfume Atomizer, three inches from top to tip which contains a quarter of an ounce of any one of six fragrances. The atomizer is a completely leakproof delicate gold cylinder, said to be permanently air tight.

Corday Perfume Atomizer

Bubble Bath Circus Wagon

The Glenway Company, Glendale, Calif., has repackaged its bubble bath in a family of three circus wagon cartons designed and made by Angelus Paperbox division of Robert Gair Co. A truck and two trailers, with cut-out wheels, have die-cut holes so that all three can be tied together to form a circus train.

Several "foamy" animals are depicted on each of the three cartons, and drivers and helpers appear in the truck. Cartons are printed red, yellow and blue plus overprinting, giving a six-color effect.

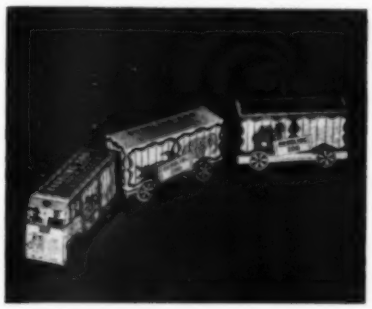
The cartons have re-use value as a toy, while the three different styles encourage multiple purchase in order to secure the complete circus train.

New Chessmen Package

Chessmen Toiletries for Men has repackaged its line in flat square glass bottles with golden caps. The famous Chessman trade mark of the Knight of Chess is fired on the bottles, and is maroon in color to harmonize with the bronze-gold linen-weave boxes.

Two exceptions are the Spray Deodorant and After Shave Powder which are in ivory plastic squeeze bottles.

Chessmen Toiletries for Men



Glenway Co. Circus Wagon

Toothbrush-Container Ships

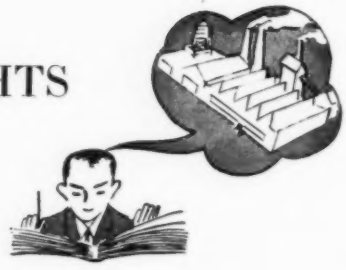
Pro-phy-lac-tic Brush Co. is packaging sets of three children's toothbrushes in separate vacuum-formed containers of Celanese acetate sheeting. Each container is in the form of a ship—an aircraft carrier, transport or a submarine—with the tops in bright solid color of red, blue or yellow.

Pro-phy-lac-tic Brush Co. Containers

Patent THOUGHTS AND TRENDS

*by Thomas Cifelli, Jr.**

PATENT ATTORNEY



Some interesting patents have been granted recently. Colgate-Palmolive succeeded in obtaining a patent (U.S. 2,689,170) on its Gardol anti-enzyme preparations. Permachem Corporation of New York obtained a patent on the idea of providing self-sterilizing materials such as fabrics, rubber goods, paper, leather, etc. (U.S. 2,689,809). The old stand-by permanent waving art continues to be active patentwise, Gillette and Lever Brothers each having obtained patents in this field, Nos. 2,688,972 and 2,689,815, respectively. Procter and Gamble came up with U.S. 2,686,761 dealing with a high water-content and high salt content milled soap, (U.S. 2,686,761).

Colgate's Anti-Enzyme Patent

It has been about a year since the sarcoside anti-enzyme tooth paste story broke wide-open. The September 1953 issue of This Journal pointed out that the only patents in this field found after considerable effort were two South African patents, Nos. 16272 and 17041, owned by Colgate. Indeed, because of the wide interest in the subject at the time, the entire text of South African patent 16272 was carried in the September 1953 issue.

It can now be said that Colgate has obtained very broad protection in the U. S. on the use of Sarcosides as anti-enzymes in dental preparations.

Although the disclosure in the U.S. patent appears to be more extensive and detailed than was the case with regard to the South African patents, the latter contained the "meat" of the story and it is believed that reference to the September 1953 issue for the disclosure will give an accurate idea concerning the situation. However, for those who wish to pursue the matter more thoroughly, a copy of the U.S. patent can be obtained for 25 cents by writing to the Commissioner of Patents, Washington, D. C.

*Newark, New Jersey.

Self-Sterilizing Fabrics

Frank Fessler, the Permachem inventor, points out that the treatment of various articles such as those made of fabrics, rubber goods, paper, leather, felt, synthetic organic plastics, ceramics, and other materials to render them lethal over prolonged periods of time and use to microorganisms coming into contact with them has been a thorny problem for some time. Methods have been devised for impregnating fibrous and non-fibrous articles with solutions or suspensions of germicides or fungicides to give a measure of self-sterilization until the fabric is used. Bandages supporting germicides on the fibres and in the interstices between the fibres have been prepared which could be stored in the open air without becoming unduly contaminated with microorganisms and which could subsequently be applied to open wounds without danger of carrying air-borne infections into the wound. According to Fessler, although this procedure has met with some success the practice has not been entirely satisfactory for a number of reasons and has not been used on a wide scale, the usual practice in the case of bandages which are to be stored prior to use being to package the sterilized bandage under aseptic conditions in a germ-proof package or to sterilize the bandage, e.g. by heat after it is packaged. Fessler points out that most of the attempts heretofore made to render fabrics self-sterilizing have been confined to the treatment of bandages and surgical gauze because of the particular necessity for keeping them in a sterile condition until used. Such articles are generally used only once and then discarded so that the question of permanence of the treatment during repeated use and laundering of the article does not generally arise. There are, however, many other instances where the need is apparent for an antiseptic and self-sterilizing cloth or other article which will retain their properties after continued and repeated use and laundering. Thus, clothing, underwear, bedding, stockings, paper, leather goods, towels, shoe linings, diaper cloth, rubber goods, bristles, plastic articles designed for body contact and many other articles invariably carry many kinds of bacteria on their surfaces after even brief exposure to the air and may become potent sources of infection when worn or otherwise contacted with the skin. Bacteria already present on the skin may be picked up by clothing and transported to abraded areas with the consequent development of infection in such areas. Frequent laundering or cleaning of such articles serves to clean and sterilize them temporarily but such sterilization has no lasting effect and the articles are subject to re-con- and thear ticles are subject to recontamination immediately after laundering.

Fessler states that there is a need for methods for treating articles so as to impart to them highly effective antiseptic and self-sterilizing properties which are not unduly affected or destroyed by laundering or cleaning or by normal use, and which would thus be effective over a long period of time in devitalizing microorganisms coming in contact therewith. It is likewise apparent that not only would the method itself be of great value, but that the self-sterilizing article itself would be equally valuable provided its self-sterilizing property were sufficiently permanent.

Fessler claims that an unexpectedly high degree of self-sterilization of a substantially permanent nature for all practical purposes can be imparted to any fibrous and non-fibrous articles by co-precipitating, under controlled conditions hereinafter described, on the surface of or in the interstices of, or even within the body of, the article a mixture of at least two water-insoluble salts or compounds, one of which is a water-insoluble silver compound. The treated article can be stored or used without

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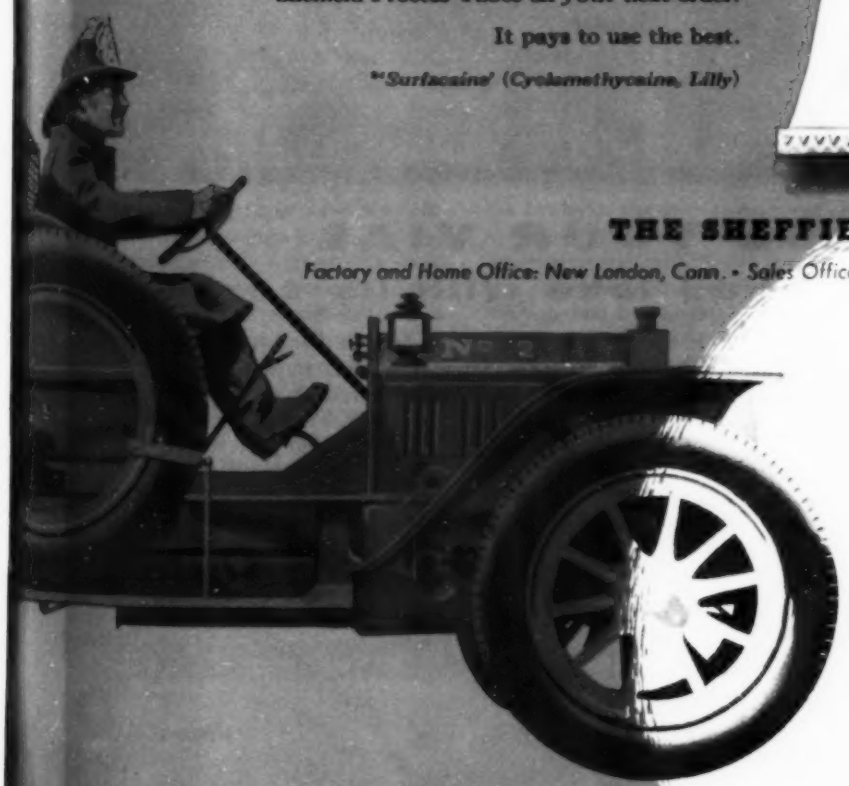

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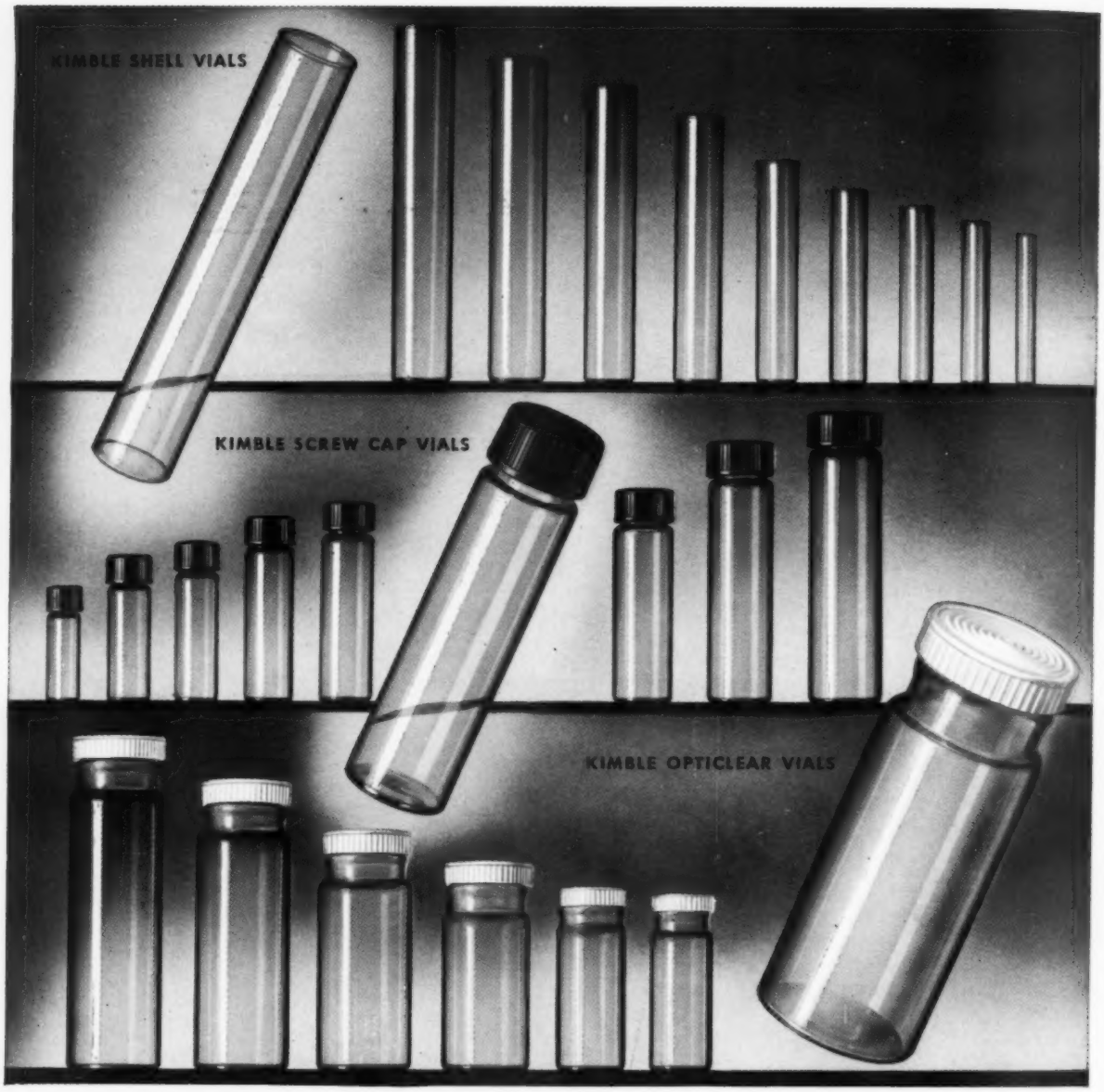

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substantial noticeable alteration in its physical characteristics as compared with the untreated article. Articles treated according to the method can be laundered or cleaned repeatedly, generally with not more than a slight diminution of their antiseptic and self-sterilizing properties. Hypochlorite and chlorine bleaching of laundered treated articles can be effected without harm and actually appears to restore any decreased germicidal activity which may have been caused by repeated laundering under adverse conditions.

A feature of the Fessler process is the presence in the precipitating bath of a compound or substance, herein referred to as a "solubilizer," which has at least a partial solubilizing effect on the water-insoluble silver compound to the extent that it renders the silver compound more soluble in the bath than in pure water. Solubilizers which can be used include ammonia and organic amines as well as certain inorganic salts. Depending upon its nature, the solubilizer is eventually removed from the article by evaporation or leaching with water, or sometimes by neutralization, leaving the co-precipitated salts dispersed in what appears to be substantially molecular interdispersion and in a form wherein they are not only extremely difficult to remove from the article but wherein the water-insoluble silver salt is substantially insensitive to discoloration by light.

Details of example 1, taken from the patent are reproduced below:

A first solution was prepared by dissolving 10 grams of silver nitrate and 20 grams of hydrated magnesium nitrate in 1000 milliliters of distilled water. A second solution was prepared by dissolving six grams of sodium chloride, 30 grams of disodium hydrogen phosphate (Na_2HPO_4:$12H_2O$) and 200 milliliters of aqua ammonia in 800 milliliters of distilled water. A sample of white cotton sheeting was immersed for a period of 30 to 60 seconds in the first solution and then removed and squeezed tightly to eliminate excess solution. The squeezed cotton sheeting contained about 150 per cent, based on its dry weight, of solution. The still wet cotton sheeting was then immersed in the second solution for 30 to 60 seconds and then removed, squeezed and dried thoroughly. The dried cotton sheeting was then washed in clear water to remove excess soluble salts and again dried. The product prepared in this manner was found to be both antiseptic and self-sterilizing. It had a hand and feel substantially identical with that of untreated cotton sheeting which had been washed in clear water and dried. The color of the treated fabric was indistinguishable from that of washed untreated fabric. Samples of the treated cotton sheeting exposed to strong sunlight daily for as long as 60 days showed no tendency to become discolored.

A number of samples of the treated cotton sheeting were washed repeatedly in a home washer using a good grade of soap and with the washing bath at about 90° C. The samples were rinsed and dried after each washing. After each period of several washings, one or more of the samples were removed and tested for antiseptic and self-sterilizing properties. After as much as 100 washings and drying cycles the samples still had significant and adequate antiseptic and self-sterilizing properties.

The experiment was duplicated with the cotton sheeting being replaced with cotton gauze, woolen uniform cloth, woolen cloth for civilian use, blended wool and cotton cloth, woolen blankets containing both virgin wool and reprocessed wool, acetate rayon fabrics, surgical masks, sugeons' hats, filter paper, cotton diapers, and woolen, cotton and acetate rayon socks and underwear. In each case the treated product was antiseptic andself-sterilizing, was substantially unchanged in its hand and feel and was not discolored by prolonged exposure to light. In the case of heavy fabrics, such as wool blankets, the samples were soaked in each of the separate solutions for about two minutes. A number of the treated fabrics mentioned were laundered and dry cleaned repeatedly without lowering their antiseptic and self-sterilizing properties appreciably.

Variations of the process were carried out by drying the final washed product in an oven at 60°-70° C., by drying the article after wetting with the first solution and before wetting with the second solution, and by carrying out the dipping steps with the first solution heated at 60°-80° C. None of these variations in the process produced any significant change in the treated article. It was noted that at higher dipping temperatures, e.g. at about 80°-100° C., a small amount of a dark precipitate gradually formed in the first solution upon prolonged exposure to light.

In still other variations of the experiment the squeezing of the sample after wetting with the first solution was varied so as to leave as little as 100 per cent or as much as 200 per cent of the first solution, based on the dry weight of the sample, absorbed on the sample. No significant differences in the results were noted.

Permanent Hairwaving

The Gillette hairwaving process which does away with the need of a neutralizer is covered by U. S. 2,688,972.

The inventor, Alfred E. Brown, points out that the neutralization step is a troublesome feature of cold wave treatments, both because it involves considerable work by the user and because the wave may be seriously impaired unless the neutralization is carefully and properly done. Aside from the natural impatience of the user to get the job done, Brown points out that there is an inherent difficulty in penetrating a wet wrapped tress with the neutralizing solution and consequently an insufficient amount of the neutralizer penetrates to the tips of the tresses causing undue relaxation of the ringlet curl.

Brown states that his invention stems from the fundamental discovery that it is not necessary that the disruption of the disulphide linkages in the hairkeratin occur at the same time that the wave is developed. Brown has found that it is possible to develop the wave as a second step following substantially complete arrestment of the chemical breakdown action.

In the Brown process, the reducing chemical is applied to the hair as before, but is left on the hair in full strength for substantially less time-seldom, if ever, for more than half of the time previously considered necessary for home waving. Then, before full development of the final wave, the solution is diluted in situ on the hair, which may be wound or curled either on rods or in a pin-curl configuration, the degree of dilution being such as to preclude further substantial reducing or chemical action on the hair. The hair with the diluted solution thereon is maintained on the curling rods or in the pin-curl configuration through a period of time sufficient to fully develop the wave and to insure substantially complete restoration of the normal disulphide linkages through aerial oxidation, the wound hair during this period being kept adequately open to the atmosphere. As the final step of the process, the hair is unwound and, if it is not already dry, wrapped into pin curls for any desired style.

Brown singles out as the important differences between his invention and prior processes, the fact that he dilutes the reducing chemical prior to full de-

(*Continued on Page 552*)

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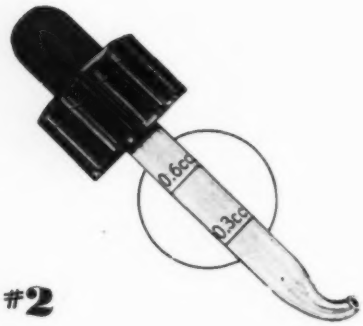

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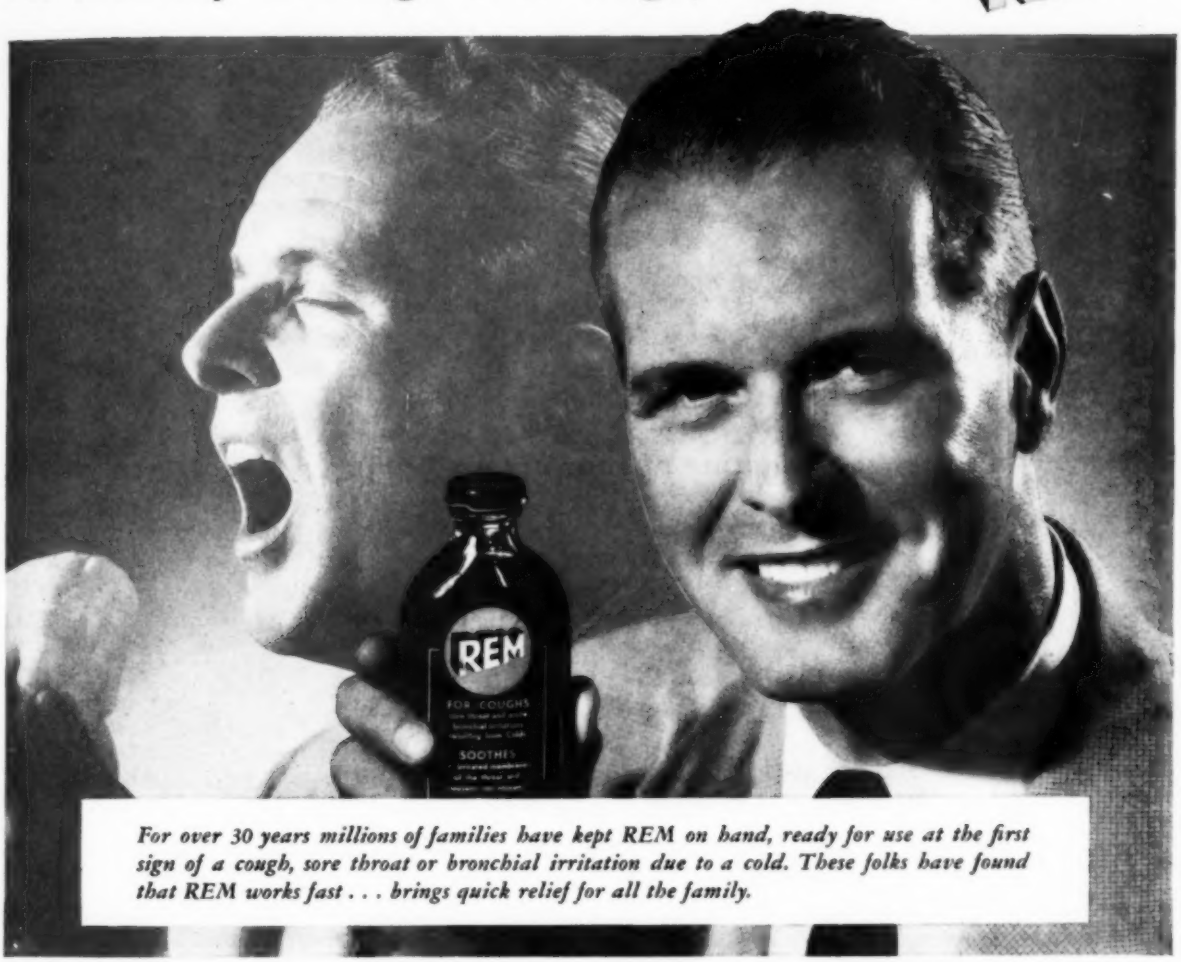

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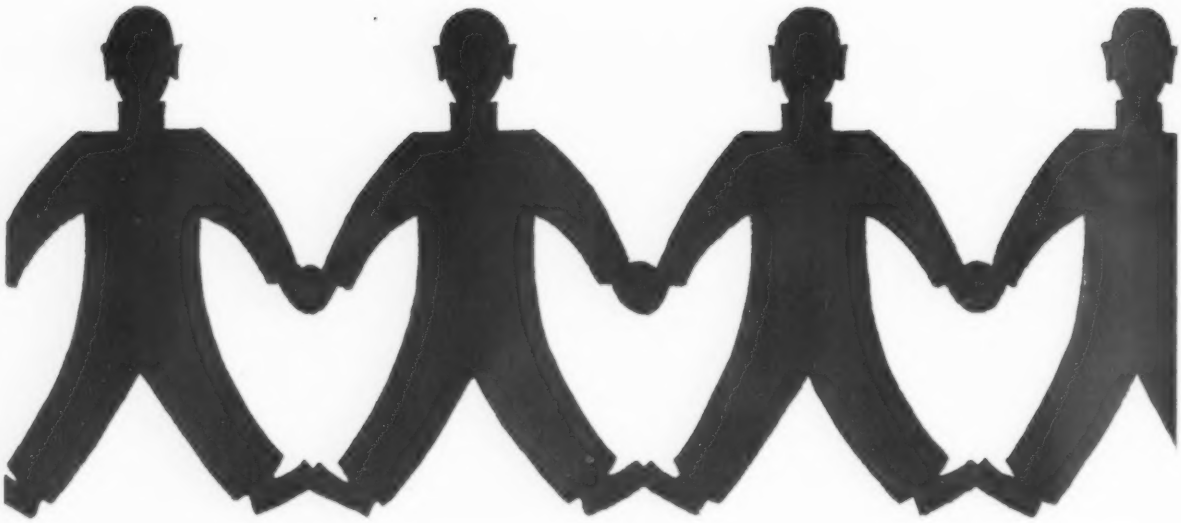

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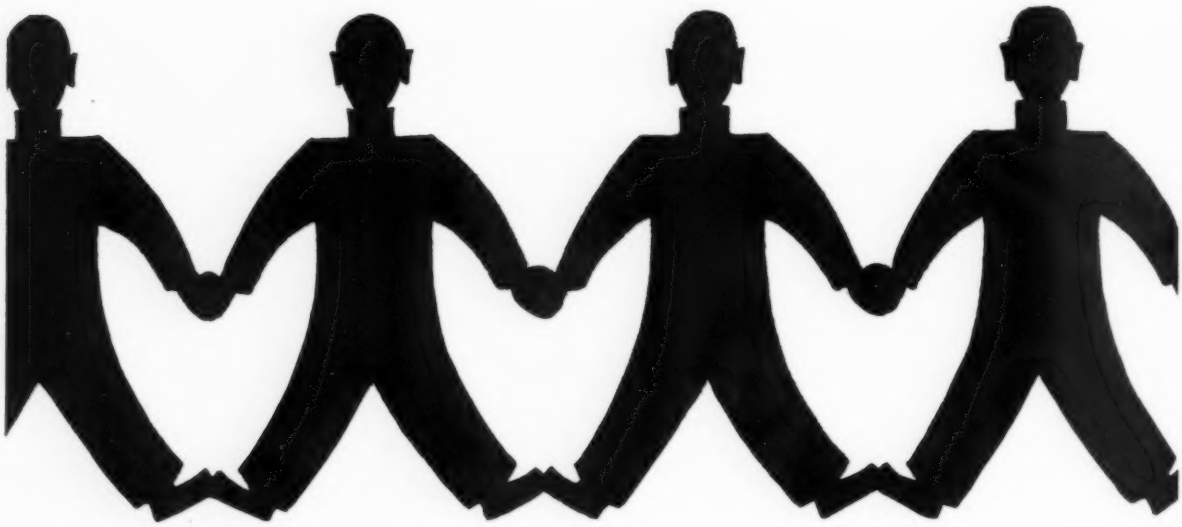

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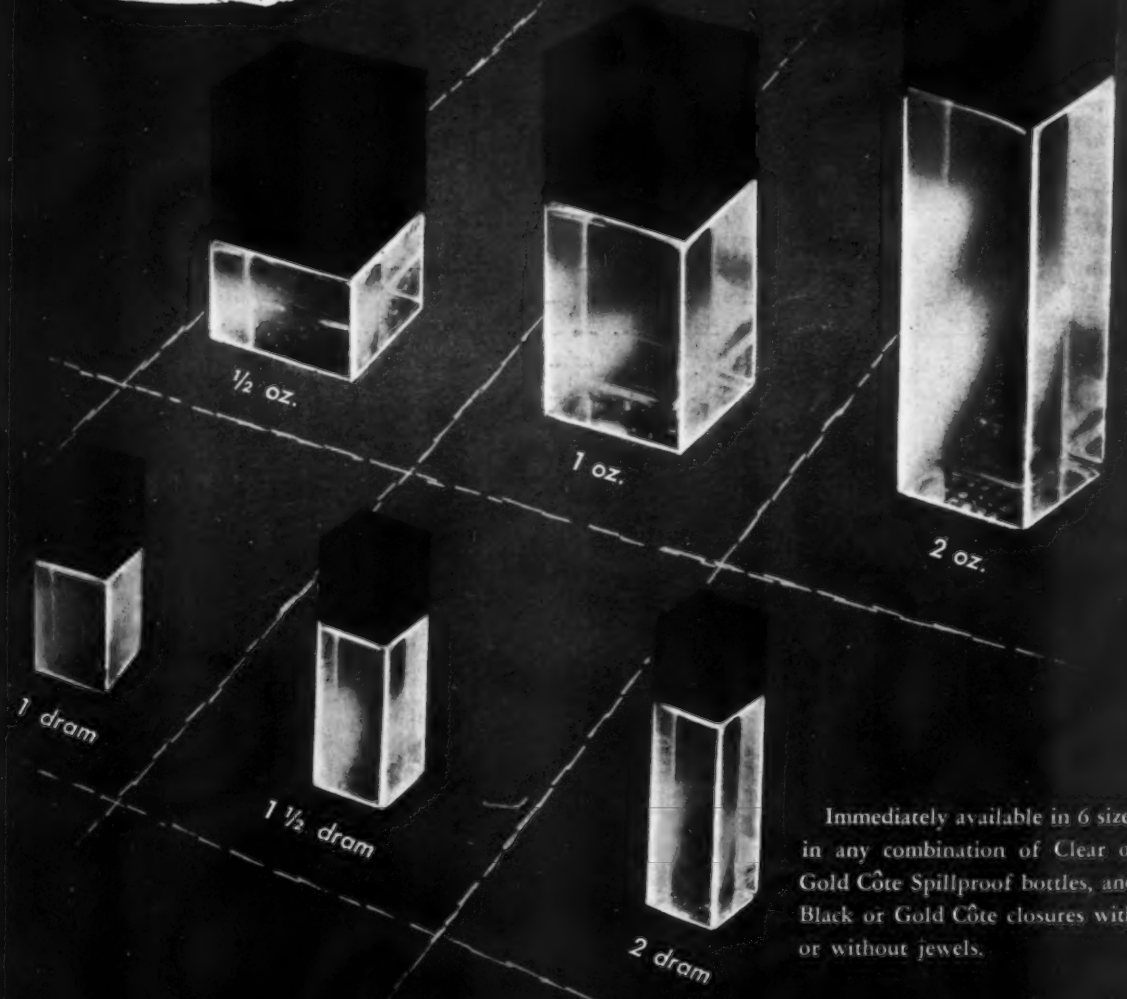

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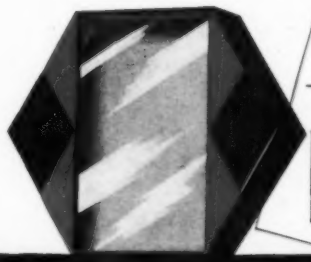

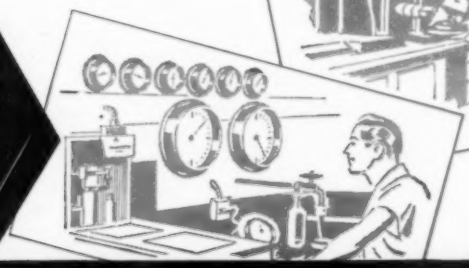

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Hanford, DCAT Chairman

Claude A. Hanford, president of Pharmaco, Inc., was elected the 58th chairman of the Drug, Chemical and Allied Trades section of the New York Board of Trade (DCAT) at its 64th annual convention at Pocono Manor, Penna., from September 23 to 25. Additional officers elected were Sydney N. Stokes, sales manager, northeastern division, Merck & Co., as vice-chairman; David Hayden, eastern sales manager, R. P. Scherer Corp., treasurer; James G. Flanagan, vice-president, S. B. Penick & Co., counsel; and Helen L. Booth, secretary.

CLAUDE A. HANFORD

Hugh S. Crosson, retiring treasurer, was elected an honorary member of the executive committee in recognition of his 13 years of service to the section.

The following, excluding officers, were elected members of the executive committee: Frank F. Black, Chas. Pfizer & Co.; Francis C. Brown, Schering Corp.; Ralph A. Clark, J. T. Baker Chemical Co.; Griffin Crafts, J. W. Wilson Glass Co.; Harold F. Cummings, Vitamerican Oil Corp.; James Day, the Dow Chemical Co.; W. T. Halsted, Thos. Leeming & Co., Inc.; William W. Huisking, Chas. L. Huisking & Co., Inc.; Louis E. Kalty, Progressive Drug Co.; George H. McGlynn, Magnus, Maybee & Reynard, Inc.; W. Boyd O'Conner, Ayerst Labs. Div., Amer. Home Products Corp.; Wm. J. Schieffelin, III, Schieffelin & Co.; F. M. Schwemmer, Ruthrauff & Ryan, Inc.; Fred G. Singer, E. I. du Pont de Nemours & Co. Inc.; J. A. Singmaster, Jr., Monsanto Chemical Co.; and Stephen F. Urban, E. R. Squibb & Sons.

Tech. Director, Warner Hudnut

Dr. Ulrich V. Solmssen has been appointed technical director of Warner-Hudnut International, according to Alfred E. Driscoll, president of Warner-Hudnut Inc. He will be responsible for new product development in foreign markets and for facilitating the exchange of scientific information between the domestic and overseas branches of the company. Dr. Solmssen has been with the company since 1946 and previous to this appointment, had been administrative director of the Warner-Chilcott Research Laboratories.

DR. ULRICH V. SOLMSSEN

Bischoff Award to Reinhold

Dr. John G. Reinhold, noted for his outstanding research in the field of liver diseases, received the 1954 Ernst Bischoff Award of $500 on September 16 at the sixth annual meeting of the American Association of Clinical Chemists at the Hotel McAlpin. The meeting was held in conjunction with the American Chemical Society.

Dr. Reinhold is associate professor of physiological chemistry in medicine at the Graduate School of Medicine, University of Pennsylvania, and is in charge of chemistry at the Pepper Laboratory of Clinical Medicine at that institution. He is chairman of the committee on clinical chemistry of the American Chemical Society and is a past-president of the American Association of Clinical Chemists.

Powers in Pharmacy Post

Wilbur E. Powers, secretary of the New Jersey Board of Pharmacy since 1945, has succeeded the late John Donahue as assistant to Executive Vice-president Newell Stewart. He will continue to serve as secretary of the Board during the current fiscal year on a part-time basis until such time as a replacement can be found.

Mallinckrodt Appointments

Charles L. Crump has become western division sales manager in charge of laboratory chemicals, Mallinckrodt Chemical Works. He will take over part of the responsibilities of Warren F. Michener who formerly supervised western division reagent chemicals sales. Mr. Michener is now temporarily in charge of the Mallinckrodt Chicago office.

William W. Scott, who joined the company in 1945, has been appointed assistant western division sales manager in charge of laboratory chemicals.

VERNON B. TUCKER

Drug & Chem. Elections

Vernon B. Tucker was elected president for the 1954-55 season of the Cincinati Drug and Chemical Association at a recent meeting. He is the Cincinnati district manager for Mallinckrodt Chemical Works.

Other officers elected were J. R. Harrington, Monsanto Chemical Co., vice-president; S. E. Spencer, Jr., Wm. S. Merrell Co., secretary; and Frank Jones, Monsanto Chemical Co., treasurer.

Schinz to Get Fritzsche Award

Dr. Hans Schinz, Federal Institute of Technology, Zurich, Switzerland, was chosen as the 1955 recipient of the Friztsche Award at the general meeting of the American Chemical Society on September 13 in New York.

This $1,000 cash and gold medal award which is donated annually by Fritzsche Brothers, Inc., will be presented to Dr. Schinz at the Society's spring meeting.

Snyder Named Research Dir.

Dr. Eric G. Snyder has been appointed research director of Shulton, Inc., according to George L. Schultz, president. He had previously been vice-president and director of research for Takamine Laboratories.

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PRECIPITATED CALCIUM CARBONATE U.S.P.

For Dentifrices—Sturge PCC stabilizes your glycerine-water mixtures. Gives you a mild controllable detergent free from grit and taste.

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For Powders—The ideal ingredient with a soft matte finish and fine texture. It maintains the delicacy of your scent. And you can be sure of uniform color.

For Fillers—To fill or pigment your lipsticks, creams and skin preparations.

The producer, John & E. Sturge, Ltd., of Birmingham, England, will meet your special density requirements. For a sample and further information write on your company letterhead to H. J. Baker & Bro.

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Squibb Lab., Colombia

A new E. R. Squibb & Sons manufacturing laboratory is now in operation at Cali, Colombia, and is producing a wide range of products, ranging from household items to antibiotic preparations. The opening of the laboratory was attended by the Colombian minister of health, the governor of the State of Valle, and some 400 additional guests, some of whom were flown to Cali from Bogota especially for the occasion.

The 53,000 - square - foot "Edificio Squibb" is constructed of reinforced concrete of the "flat slab" type and designed so that it can be expanded when the need arises. Manufacturing and storage areas are air conditioned, and humidity control apparatus has been installed where necessary. The section which handles antibiotics has its air continuously sterilized by ultraviolet lamps. None of the windows in the building open, thus avoiding dust and other contamination from the outside.

New manufacturing laboratory of E. R. Squibb & Sons at Cali, Colombia. The 53,000 square-foot building is designed so that it can be expanded when it becomes necessary. Underground facilities include ramp for trucks, as well as workshops, boilers, generators and similar equipment.

Bell, Pres. of Pharma-Craft

Frank F. Bell, formerly vice-president in charge of sales and advertising of Grove Laboratories, has been elected president of Pharma-Craft Corp. He succeeds Charles A. Howell who has retired.

FRANK F. BELL

San Filippo with Bradley

Robert D. San Filippo, formerly with Pan-American Airlines, has been named manager of the contract packaging department of the Bradley Container Corp., according to Bradley Dewey, president.

Wade Named Sales Supervisor

Michael W. Wade has been appointed field sales supervisor in the Bristol division of the S. E. Massengill Co. He was formerly detail sales representative for the company.

Parkview Drugs Gives Dinner

Phil Small, president of Parkview Drugs, and the Blanchard Perfume Co. were hosts to 150 guests on Tuesday, August 31, at a dinner at the Wishbone Restaurant in Kansas City. Guests included Parkview managers, assistant managers, cosmetic department personnel and personnel from Parkview's Topeka drug stores.

Miller Named Pres., PMMI

Tom Miller, vice-president of Package Machinery Co., has been elected president for the ensuing year of the Packaging Machinery Manufacturers Institute.

TOM MILLER

Talks Before A.C.S. Meeting

Dr. Edward A. Schildknecht, organic chemist of Dodge & Olcott, Inc., delivered a paper before the American Society on September 16 during the organization's annual meeting. Entitled, "Synthesis of 2-Thiophene Analogs of Amidone and Isoamidone," the paper described the work done by Dr. Schildknecht and Dr. Ellis V. Brown of Seton Hall University in synthesizing the 2-thiophene analogs of these two compounds.

Olin Mathieson Elections

Officers of Olin Mathieson Chemical Corp. were elected last month, following the merger on August 31 of Olin Industries, Inc., and Mathieson Chemical Corp., according to John M. Olin, chairman of the board, and Thomas S. Nichols, president. Those elected included John W. Hanes, chairman of the finance committee and vice-president for finance; and F. Stillman Elfred, John C. Leppart, and Stanley de J. Osborne, as executive vice-presidents.

Russell R. Casteel has become vice-president; Norman H. Collisson, Donald W. Drummond, R. L. Hockley, Milton F. Meissner, S. L. Nevins and J. J. Toohy, vice-president for operations; Russell Hopkinson, vice-president for development; Robert W. Lea, vice-president for organization; R. B. Lewis, vice-president for financial analysis; David T. Marvel, vice-president for sales; Walter F. O'Connell, vice - president and assistant to the vice-president for finance; Fred Olsen, vice-president for research; Ralph A. Ostberg, vice-president for production; Theodore Weicker, Jr., vice-president for overseas operations; Edgar W. Taft, treasurer; C. C. Tallman, comptroller; Gordon Grand, Jr., secretary; E. R. Van Vliet, assistant treasurer; and A. P. Winsor, assistant secretary.

These officers were all formerly associated with one or the other of the predecessor companies.

Reznek with Research Inst.

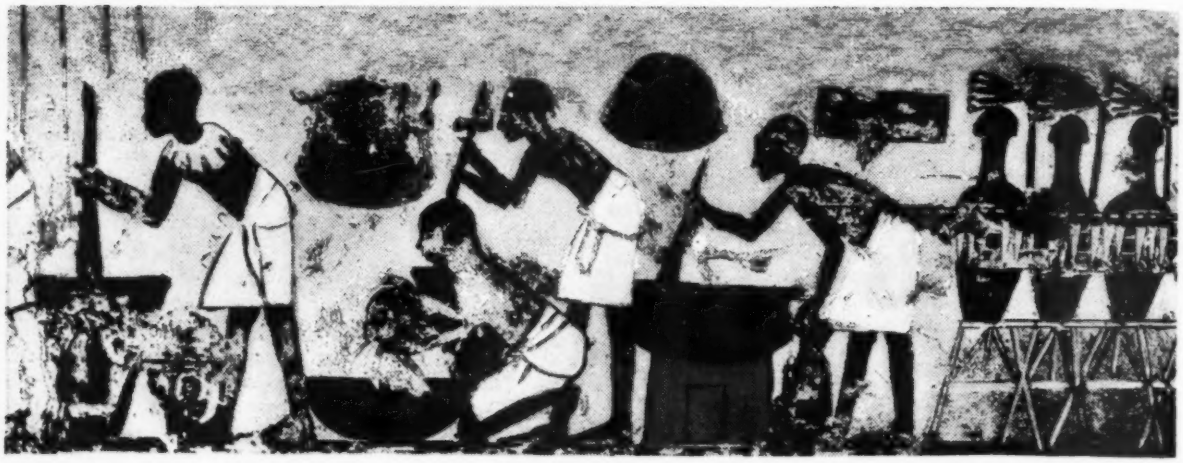
Dr. S. Reznek has been assigned to the pharmacy department of the Sterling-Winthrop Research Institute, according to Dr. M. L. Tainter, director. He had formerly been director of control at Cook-Waite Laboratories, Inc.

FLA.

75, 4

No. 4 of a series

The Origin of FLAVORED MEDICINALS



Egyptians preparing ointments. Courtesy J. B. Lippincott Co.

One of the oldest medicines and spices—still in wide use today, ANISE, was obtained by the ancients primarily from Crete and Egypt. Source of many a popular taste-treat including cordials and candies, this aromatic spice oil finds extensive application as a flavoring agent for pharmaceutical products. Due to current scarcity of the natural oil, synthetic products and Anethole, a domestically produced aromatic, are in widespread use. The D&O Flavor Laboratories have developed a large variety of compounds for flavoring pharmaceuticals based on the venerable and versatile Anise. Consult D&O.

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ESSENTIAL OILS • AROMATIC CHEMICALS • PERFUME BASES • FLAVOR BASES • DRY SOLUBLE SEASONINGS

New Research Lab. for Allied

Allied Chemical & Dye Corp. dedicated the new Research laboratory for its General Chemical division in Morris Township, N. J., on September 8. Members of the laboratory supervisory staff conducted guests on guided tours of the $2-million construction during the open house ceremony.

The three-storey; L-shaped building provides over 55,000 square feet of floor space for research activities, including more than 30 laboratories, a technical library and engineering research offices, as well as a special section for work with radio-active substances.

This research laboratory replaces the division's Laurel Hill, Long Island, unit which was one of the first major chemical research centers in the country.

Dr. J. H. Pearson, a member of the General Chemical research staff for the past 18 years, is director.

Schoettle Co. Sold

Heirs of Edwin J. Schoettle, Philadelphia, have relinquished their interests in the Edwin J. Schoettle Co., one of the nation's oldest and largest folding box manufacturers, and its subsidiaries, according to Douglas T. Neale, president. Ownership was acquired by Mr. Neale and principals of United Container Co., Kardon Box Co., and Philadelphia Container Co., all of Philadelphia.

Douglas T. Neale, who will continue as president of the company, declared there will be no change in management, personnel or established policies of the organization.

Hartwell with Vick Chemical

John M. Hartwell, formerly controller and secretary of Electronic Products Corp., has joined the Vick Chemical Co. as special assistant to Donald B. Woodward, chairman of the finance committee.

Allied Chemical & Dye Corp.'s newest research laboratory which was opened Sept. 8 by its General Chemical division in Morris Township, N. J.

Stauffer Wins 1st Prize

Stauffer Chemical Co., Columbian Carbon Co. and the Dow Chemical Co. last month received awards in the "Best Place to Work" competition sponsored by *Management Methods* magazine. The competition was designed to demonstrate how well-planned, well-integrated quarters improve both employee and executive productivity and morale.

Stauffer won first prize for its new main offices at 380 Madison Ave., New York, as the "Best Integrated General Office." The company also won a special award for the "Best Employee Lunch/Lounge Area."

Columbian Carbon and Dow Chemical received Special Awards for the "Best Board or Conference Room," and the "Best 'Special Situation' Solution," respectively.

Named Koster Keunen Rep.

Koster Keunen, Inc. has appointed R. E. Flatow & Co. as its representative on the West Coast for the sale of beeswax, ozokerite and ceresine.

Nichols in Rhodia Exec. Post

H. C. Nichols, formerly with the Engineering Corp. of America, has been appointed head of the Engineering Service Section of the Industrial Redolorants division of Rhodia, Inc.

Polyclosure Corp. Formed

The Polyclosure Corp., 111 Fifth Ave., New York, was organized last month for the manufacture and distribution of polyethylene containers for rectal and vaginal suppositories. This plastic enclosure is said to have many advantages over the old tin foil wrapping method, in that it is protected from adverse weather changes such as heat, cold, humidity and moisture. The manufacturing process is patented, and the exclusive rights and distribution have been obtained by the Polyclosure Corp.

President of the company is F. A. Scervini, while Eugene Alaimo is secretary-treasurer.

Court with Klein Inst.

Donn R. Court has left the post of vice-president in charge of sales and advertising, Cutter Laboratories, to join the Klein Institute for Aptitude Testing, Inc., as vice-president in charge of a newly opened western branch at 300 Montgomery St., San Francisco.

Patten Named Sales Manager

William T. Patten, formerly assistant advertising manager and assistant sales manager, has been appointed sales manager of the Chattonooga Medicine Co., succeeding A. L. Grey who has retired.

JOHN M. HARTWELL

H. C. NICHOLS

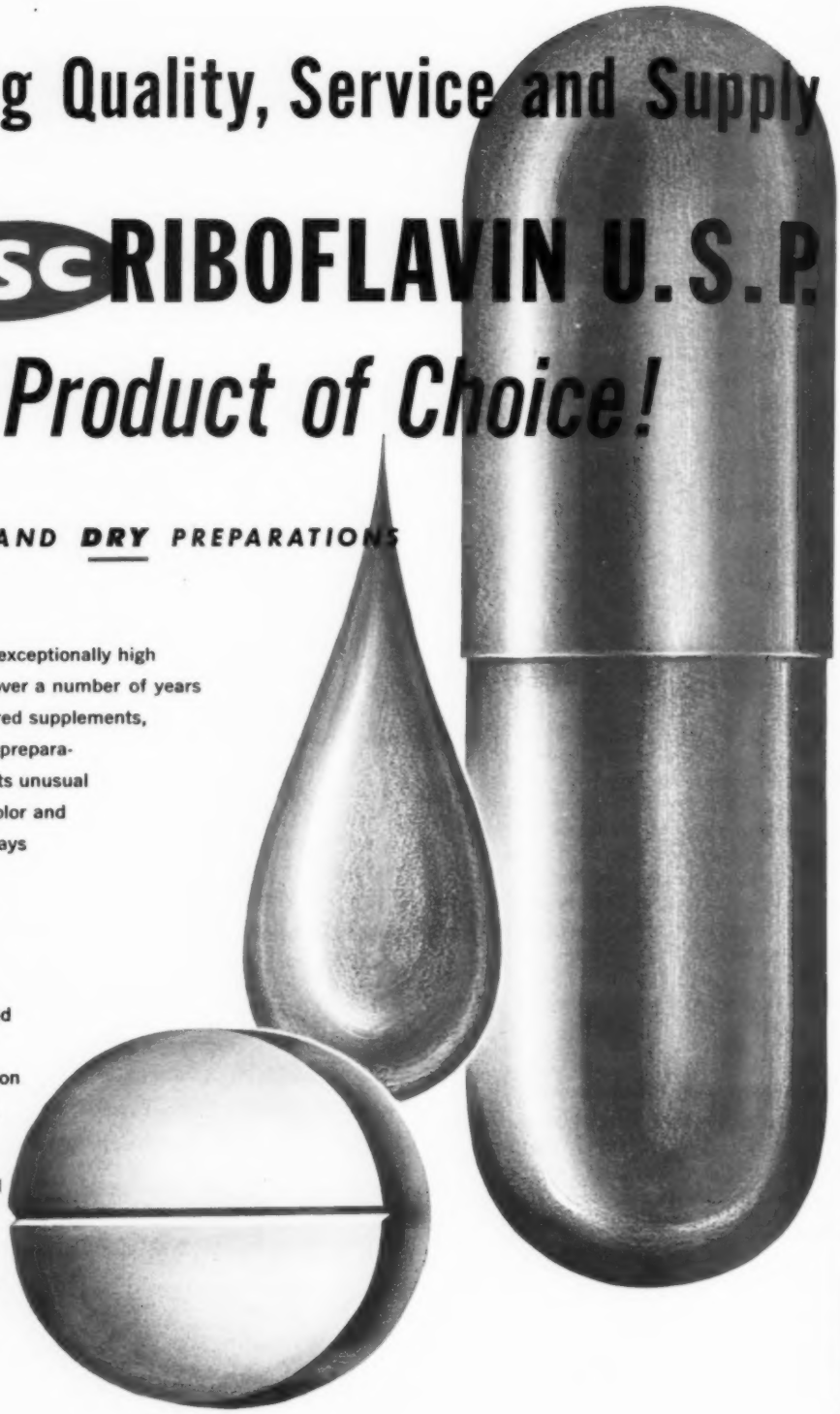
WILLIAM T. PATTEN

Outstanding Quality, Service and Supply

make CSC RIBOFLAVIN U.S.P.

the Product of Choice!

FOR BOTH LIQUID AND DRY PREPARATIONS



CSC Riboflavin U.S.P. is a product of exceptionally high purity. It has found wide acceptance over a number of years for elixirs, injectable solutions, powdered supplements, multi-vitamin drops, capsules and dry preparations. It is non-hygroscopic and exhibits unusual uniformity of crystals. Uniformity of color and complete freedom from odor have always been outstanding characteristics of riboflavin produced by CSC's unique quality-controlled process.

Since CSC is a primary producer of this important product, you are assured of a constant supply at all times—quickly furnished you from a distribution point located nearby. Available in 100, 1000 and 5000-gram containers.

Samples available as well as a detailed TECHNICAL DATA SHEET. Write for yours today on your company letterhead. Industrial Chemicals Sales Dept., Commercial Solvents Corp., 260 Madison Ave., New York 16, N. Y.

COMMERCIAL SOLVENTS
CORPORATION

Package Machinery to Buy

The Package Machinery Co., East Longmeadow, Mass., has offered to purchase the Reed-Prentice Corp. of Worcester, Mass., according to Roe S. Clark, president of Package Machinery, and Frederick W. McIntyre, Jr., president of Reed-Prentice. Negotiations have been completed in which Package Machinery, subject to the fulfillment of certain conditions, is offering to purchase the common stock of Reed-Prentice Corp. from its stockholders at a price of $12 per share.

Armour Labs. Appointments

Craig S. Rice, formerly a market analyst, Armour Laboratories, has been named manager of the market research department, according to Edgar L. Patch, general manager.

Billy E. Clabb, assistant division manager of the southwest division of Armour Laboratories, has been promoted to division manager of the Pacific Coast division, with headquarters at San Francisco.

Durrer Returns to U.S.

E. R. Durrer, president of the Givaudan Corp. and its associate companies, last month returned to the United States from a 3-month European trip. He visited the Givaudan factories in Switzerland and France and renewed acquaintances with members of the European industries served by Givaudan whom he had not seen in several years.

Murphy with Gair

Homer Murphy has been appointed sales manager of Robert Gair Company's Angelus Paper Box division, according to Jack Hendricks, general sales manager.

Breck Sponsors Concert

A Pops concert, called, "The Anniversary Pops Concert," sponsored by John H. Breck Inc., was presented Sunday evening, August 22, in the Grand Ballroom of Chicago's Conrad Hilton Hotel, for 1100 members and guests of the Beauty and Barber Supply Institute on the occasion of the Institute's annual convention. This musical affair commemorated the 50th year of the Beauty and Barber Supply Institute and the 25th anniversary of the incorporation of the Breck Company.

The Breck Company was represented by Edward J. Breck, president and John H. Breck, Jr., executive vice-president.

Mlle. Genevieve de Galard-Terraube, "Angel of Dien Bien Phu," receiving from Lamson Scovill, president of Scovill Mfg. Co., replicas of gold buttons given to Gen. Lafayette in 1825. Scovill used the original dies to strike this set of buttons for presentation to the Republic of France through Mlle de Galard.

FRED R. WOLF

Wolf Promoted by Lilly

Fred R. Wolf, with seven years of experience in the financial division of Eli Lilly International Corp., has become general auditor of the company.

Scovill Recasts Gold Buttons

Lamson Scovill, president of the Scovill Manufacturing Co., presented a gift of thirteen solid gold buttons bearing the profile of George Washington (an exact duplicate of a "bon voyage" gift especially designed for General Lafayette by the predecessor Scovill firm in 1825) to the Republic of France through Mlle. Genevieve de Galard-Terraube, "The Angel of Dien Bien Phu," on August 16, prior to her return home. Mlle. de Galard was given a fourteenth button as a personal memento.

The inscription on the back of the original buttons, which have never been found, had read, "Presented to General Lafayette by L. H. & Scovill, Button Manufacturers, Waterbury, Conn." The firm's name at that time was Leavenworth, Hayden & Scovill.

"I am very touched by the fact," said Mlle. de Galard, "that these are exact reproductions of those which were given by your great-grandfather to General Lafayette [in 1825]. These buttons will be put in a French museum as a symbol of the friendship which has existed between the United States and France since General Lafayette and which has been reaffirmed by the warm welcome which I have received in this country."

Scovill Manufacturing Co. traces its history back to 1802 when a small metal button factory was started in Waterbury. A few years later it became the first American firm to cast brass.

Left to right: Eugene List, piano soloist; Miss Arppie Charkoudian, special mystery soloist; and Edward J. Breck, president of John H. Breck Inc., congratulating Arthur Fiedler, Conductor of Boston Pops Orchestra, at conclusion of Anniversary Pops Concert.

Winthrop West Coast Unit

Winthrop-Stearns, Inc., is building a 40,000-square-foot single-storey building as its Western headquarters in Bohannon Industrial Park, San Mateo, Calif. The Bohannon organization will own, operate and maintain the building for the firm on a long-term lease arrangement. Construction will be completed early next year.

The new building will serve as administration, distribution and warehouse center in the seven western states for Winthrop-Stearns, and for George A. Breon & Co., Cook-Waite Laboratories, Inc., and Sterwin Chemicals Inc., all units of Sterling Drug.

Architect's drawing of new West Coast headquarters of Winthrop-Stearns Inc. which will be completed early next year. Building will serve as administration, distribution and warehouse center in the seven western states for Winthrop-Stearns, and for George A. Breon & Co., Cook-Waite Laboratories, and Sterwin Chemicals Inc.

Reid Joins Squibb

Francis J. Reid, who recently resigned from New York Quinine & Chemical Works, is now associated with the Chemical Division of E. R. Squibb & Sons.

To Represent Fluid Chem.

Stanton Sales Co. and Charles A. Mooney have been retained as special representatives of the Fluid Chemical Co., according to E. Bennett, president. Stanton will cover the area from Chicago to the East Coast, and Mr. Mooney, 600 North Sepulveda Boulevard, Los Angeles, formerly president of Lentheric, Inc., will contact accounts for aerosol-filling contracts in the West Coast area.

Named Mgr., Gair Division

Frank E. Newton has been appointed manager of the Pennsylvania corrugated box division of Robert Gair Co., according to William T. May, Jr., vice-president in charge of container operations. He replaces Harry J. McPhilliamy who will act as assistant division manager, performing such duties as his health will permit.

Mr. Newton had formerly been manager of the company's Ohio corrugated box division in Cleveland.

Pittenger Retires from S & D

Dr. Paul S. Pittenger, Sharp & Dohme, vice-president since 1930 and director of quality control, retired on October 1. He joined the H. K. Mulford Co. as director of pharmacodynamic research in 1910 and held that position until 1925. Two years later he was appointed director of pharmacologic research at Sharp & Dohme which named him assistant general superintendent in 1928 and assistant to the president in 1929. Dr. Pittenger became vice-president the year following the merger of Sharp & Dohme and H. K. Mulford.

Ferment-Acid Vs. Miles Labs.

Ferment-Acid Corp., New York, has filed a patent infringement action against Miles Laboratories, Inc., demanding damages of $1 million and an injunction prohibiting use of its basic patent No. 2,353,771 covering "deep fermentation." This patent relates to methods for "deep fermentation" production of citric acid, a component of Alka-Seltzer which Miles manufactures.

Promoted by Bristol-Myers

Edmund W. Morris has been appointed brand advertising manager of Bristol-Myers products division. He has been with the company since 1946 when he joined the Rubberset division.

Ushiyama Visits Kohnstamm

Harry Ushiyama, president of Hollywood Cosmetic Co., Inc., of Japan and Hollywood, and Mrs. May Ushiyama, who operates the most exclusive beauty salon in Japan, recently visited the New York office of H. Kohnstamm & Co., Inc. They wish to increase their line of beauty preparations.

Croda Represents Protan

Croda, Inc. has been appointed exclusive sales agent by A. S. Protan of Norway, for the sale of aginates in the Eastern United States.

With Norwich 35 Years

Howard A. Sumner, assistant to the president, and Dr. D. M. Copley, chief chemist, the Norwich Pharmacal Co., have both completed 35 years of service with the firm.

Robert Visits U. S.

Henri L. Robert, technical director and perfumer of Chanel, in Paris, visited the United States last month during which time he conferred with H. Gregory Thomas, Chanel president. He was formerly in America for 11 years, having been associated with this industry as a perfumer, and prior to that, in Paris and Grasse.

W. F. George to Witco

William F. George retired from Hooker Electrochemical Company September 1. Mr. George was New York district sales manager upon his retirement caused by Hooker policy which requires retirement at a specific age. However, Mr. George is not remaining idle, and he is now associated with Witco Chemical Company, N. Y.

Tombarel to Move

Tombarel Products Corporation will move in November to new quarters at 725 Broadway, New York 3.

FRANK E. NEWTON

EDMUND W. MORRIS

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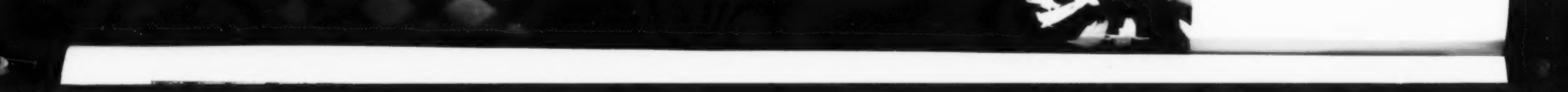
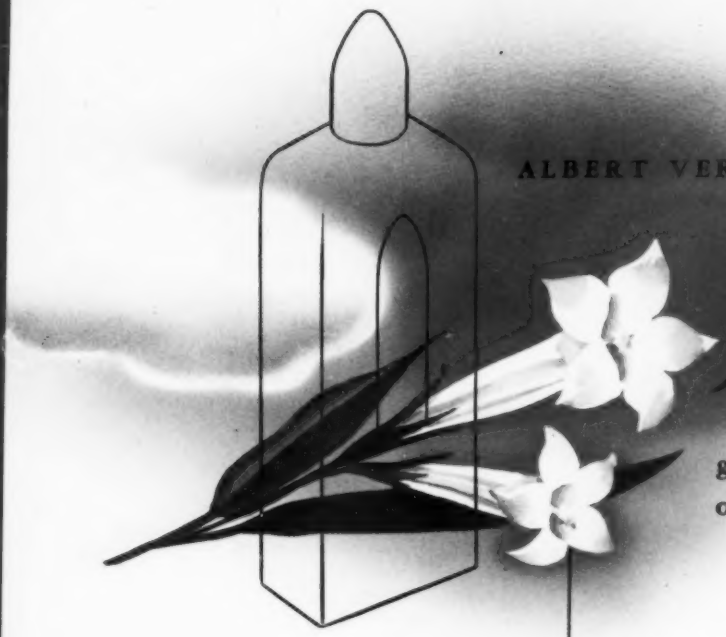


Nicotinia Verley

. . . an appealing fragrance inspired by the "Sweet Tobacco" of the old-fashioned garden

★

—TURN THE PAGE



ALBERT VERLEY & COMPANY'S

Nicotinia Verley

glorifies the early-morning sweetness of the Nicotinia Assimis fragrance

$36 per lb.

In the old-fashioned gardens of a bygone day, they planted "Sweet Tobacco" or "Shooting Star" — now technically known as "Nicotinia Assimis" — directly under bedroom windows, so that its fragrance might be wafted into the sleeping chambers during the early morning hours when it is sweetest.

Picture, if you will, a sweet, powerful blend of Jasmin, Tuberose, Carnations, and Roses — with just a bit of the pungency of the Narcisse. Nicotinia Verley is offered to you as a glorified replica of this fragrant American garden favorite. It can be used in all toilet goods.

For a new, appealing note, or inspiration to create an entirely new formula, we suggest Nicotinia Verley. Write for working samples.

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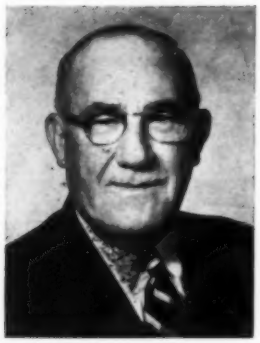
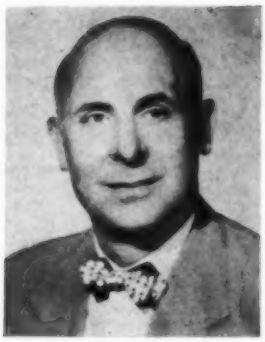
Synthetic Aromatic Products and Organic Isolates • Synthetic Flower Oils and Aromatic Bases • Bouquets and Finished Compositions

HERBERT A. STRATE



HAROLD C. GREEN



HERBERT W. DECKER

ROBERT L. RICE

MICHAEL GIRBINO

D&O Exhibit at Smithsonian

Dodge & Olcott, Inc. last month presented a specially designed exhibit entitled, "Take Away That Bitter Taste," to the Smithsonian Institution's division of Medicine and Public Health. Prepared for a place in the medical gallery where it has been installed, the exhibit traces the evolution of flavoring medicine from some of the earliest-known records to the modern laboratory where synthetics mark the farthest rise of this particular science.

Uhe Discusses Essential Oils

George Uhe, president of George Uhe & Co., delivered a talk on essential oils before the monthly meeting of the Essential Oil Association of the U.S.A. on September 14. Describing his experiences on a recent extended business trip abroad, he stated that more emphasis is being placed on the production of agricultural products for foodstuffs than on crops suitable for the distillation of essential oils.

With Burroughs Wellcome

Dr. Edgar A. Jack has been appointed a member of the medical staff of Burroughs Wellcome & Co. (U.S.A.) Inc.

Strong, Cobb Exec. Changes

Herbert A. Strate, vice-president and general sales manager of Strong, Cobb & Co., has transferred his offices from Cleveland to the Strong, Cobb plant in Hawthorne, Calif. He will direct the western states division sales for the company, according to M. M. Ricketts, president, and will also supervise the firm's national business as well as direct and establish research in new products and production for the Hawthorne plant.

Harold C. Green, formerly New York sales manager, has been appointed eastern divisional manager of the eastern states, with offices at 745 Fifth Ave., New York.

Herbert W. Decker, formerly chief pharmacist at Crile Clinic, has been named central division sales manager of Strong, Cobb.

Michael Girbino, with the company 21 years, has been appointed manager of research and control laboratories.

Robert L. Rice, formerly with the American Chlorophyll division of Strong, Cobb, has become manager of the new unit packaging division at Cleveland.

Ching, DCAT Guest Speaker

Cyrus S. Ching, chairman of the Atomic Energy Labor-Management Relations Panel and former director of the Federal Mediation & Conciliation Service, was guest speaker at the 64th annual meeting of the Drug, Chemical and Allied Trades Section of the New York Board of Trade which was held from September 23 to 25 at Pocono Manor, Penna.

Promoted by Smith-Dorsey

Thomas Watson, formerly divisional sales manager for Smith-Dorsey, has been appointed administrative assistant to the sales manager. This is a new position in the home office at Lincoln, Neb.

Wernet Promoted by P-D.

Richard Wernet has been promoted to assistant manager of the Boston branch of Parke, Davis & Co., according to Graydon L. Walker, vice-president and director of U. S. and Canadian sales and promotion. He will work under the direction of W. R. McCollam, branch manager.

Mr. Wernet had formerly been assigned to the retail sales promotion staff in Detroit.

Gilbert on Schenley Board

George R. Gilbert, vice-president in charge of international operations for Schenley Laboratories, has been elected to the company's board of directors, according to R. Blayne McCurry, president. He has been with the company for 13 years.

U.S.I. Moves Sales Division

U. S. Industrial Chemicals Co., division of National Distillers Products Corp., has moved its New York sales division offices to the National Distillers Building, 99 Park Ave., New York 16. The new telephone number is OXford 7-0700.

Mathis Heads State Pharmacal

John H. Mathis, vice-president in charge of sales and advertising, has been elected president of State Pharmacal Co.

Heyden PARASEPTS®

FUNGAL AND BACTERIAL ACTION...

Do you have a product that needs positive protection against bacterial and fungal growth? It will pay you to look into the following advantages of using Heyden PARASEPTS to preserve the quality so essential to sales and profits:

- **High effectiveness against molds and bacteria.**
- **Extremely low toxicity confirmed by extensive tests.**
- **Non-irritating to the skin.**
- **Colorless, odorless, practically tasteless.**
- **Stable during heat sterilization.**

Research has shown that a combination of two or more Parasepts gives better protection than a single ester. There are five of them available to provide the right combination for your particular product. Write for a copy of the technical bulletin giving full information. Samples available on request.

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Purified
(Methylparaben U.S.P.)

ETHYL PARASEPT
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PROPYL PARASEPT
Purified
(Propylparaben U.S.P.)

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Technical Grades also available.
100, 50 and 25-lb. fiber drums.

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McLean Named Merck V.P.

William H. McLean, vice-president for marketing, Merck & Co., for the past three years, has been appointed to the new position of vice-president and general manager of the chemical division.

He has been with the company since 1948, serving as director of commercial development and in other management capacities before becoming vice-president.

During the war, Dr. McLean was in charge of research and development, Army Quartermaster Corps, and subsequently served with the Research and Development Board of the Department of Defense.

WILLIAM H. McLEAN

Austin H. Brown

Austin H. Brown, for 36 years head of the purchasing division of Eli Lilly & Co., died September 7 at 66 years of age and had been with the company 42 years and had been active as director of purchasing until last December 31 when, for reasons of health, he asked to be relieved of the director's duties. He remained as a purchasing consultant.

Frank B. Redington

Frank B. Redington, president of the F. B. Redington Co. for 50 years, died September 23 in a nursing home. He developed the first chewing gum wrapping machine in 1897. He and his company subsequently developed cigarette, candy and other packaging devices.

Surviving are his widow, Mary K., and three nieces.

Mrs. Helene H. Pessl

Mrs. Helene Herz Pessl, founder and former president of Helene Pessl, Inc., died last month in Salsburg, Austria, after a brief illness. She was 72 years old. Mrs. Pessl came to this country in the 1930's and founded the company in 1942, from which she retired in 1947.

Surviving are two daughters, Mrs. Yella Pessl Sobotka and Mrs. Margit Pessl Cartwright; and three grandchildren.

August A. Wasserscheid

August A. Wasserscheid, who retired six years ago as Vice-president and General Manager of the Eastern Division of Mallinckrodt Chemical Works, died September 27, after a long illness. He joined Mallinckrodt in 1893, was appointed General Manager of the Eastern Division in 1913, and was subsequently appointed Vice-president. He served 55 years with the company, and was 83 years of age at the time of his death.

Mr. Wasserscheid was born in New York January 11, 1871. He was a graduate of the City College of New

AUGUST A. WASSERSCHEID

York, and of the College of Pharmacy, Columbia University, with a Ph.G. degree, in 1892.

Mr. Wasserscheid was widely known and had a host of friends throughout the drug and chemical industry in the United States. He had been an active participant in the affairs of the American Drug Manufacturers Association, the American Pharmaceutical Association, the American Pharmaceutical Manufacturers Association, the Drug, Chemical, and Allied Trades Section of the New York Board of Trade, the Federal Wholesale Druggists Association, the National Wholesale Druggists Association, the Manufacturing Chemists Association, and the National Wholesale Druggists Association. He was a past president of the Drug & Chemical Club, New York. He was a Mason and a Shriner, a member of the Garden City Country Club, and a well known philatelist, his stamps having been exhibited at many philatelic exhibits.

He is survived by his widow, the former Florence A. McKown, whom he married February 15, 1900, and by a brother, Otto Wasserscheid, Sr., Peekskill, N. Y., and a sister, Mrs. Clara Kroger, of the Bronx, N. Y.

Charles S. Campbell

Charles Soutter Campbell, who gave up a career in the ministry for business and became president, treasurer and director of the J. B. Williams Co., died September 21 at his home. He was 67 years old.

Mr. Campbell was graduated from the Yale Divinity School in 1917, but instead of following the ministry, he became assistant to the president of the Durham-Duplex Razor Co. Later he was made president of Index Invisible, Inc., which was absorbed by Remington Rand. He then became vice-president of the latter.

Elected president and director of Durham-Enders in 1926, he joined the Williams Company in 1937, shortly thereafter holding the posts of president and treasurer as well as director.

Surviving are his widow, Mary Abbe Campbell; and six children, Charles S., Jr., William P., Robert A., Mary, Mrs. Stuart Clement and Mrs. Sidney Lovett.

Charles H. Cooper

Charles H. Cooper, a partner in Cooper and Shuesler, Chicago pharmaceutical representative, died August 6 of a heart attack. He acquired his early business experience in the sales divisions of retail and wholesale pharmaceutical firms in the Midwest and West Coast. Mr. Cooper joined Charles R. Shuesler in 1916 to form the partnership. The company has represented A. H. Wirz, Inc., in the midwest territory since 1921.

Dr. Carl J. Norden, Sr.

Dr. Carl J. Norden, Sr., died in Lincoln, Nebraska, on August 21 at the age of 64. He was chairman of the board of Norden Laboratories which he founded in 1919.

He is survived by his wife, Emma, and a son, Dr. Carl J. Norden, Jr., who is vice - president and secretary of Norden Laboratories.

John E. Donahue

John E. Donahue, recently appointed secretary of the National Pharmaceutical Council, died on August 19 after a very short illness.

Surviving are his wife, Mary E. Donahue, and three children, Hugh, Elinor and James.

John F. McCambridge

John F. McCambridge, founder and president of the McCambridge and McCambridge Co., died August 28.

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Lemon Sesquiterpeneless
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Peppermint Twice Rectified (Triple Distilled) U.S.P.
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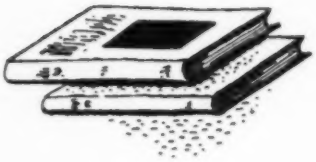

Trade Literature

Paper Box Machine

Stokes and Smith Company, 4992 Summerdale Avenue, Philadelphia 24, has issued a 2-color, 6-page brochure—Bulletin BS 501—describing the recently developed Stokesmatic fully automatic paper box machine. Stokesmatic operation includes staying, gluing, registration, feeding, and wrapping without the need of an operator.

American Cholesterol Booklet

American Cholesterol Products, Milltown, N. J., are distributing a booklet containing 20 pages of data sheets concerning their products. This will prove to be a very valuable reference book for chemists and others in this industry.

Synthetic Organic Chemicals

The Synthetic Organic Chemical Manufacturers Association, 41 East 42 Street, New York, has issued a 32-page booklet entitled Allies in Defense—Some Fact About Synthetic Organic Chemicals. This booklet will give anyone considerable understanding of the organic chemical industry and of its importance in defense in a very short time.

List of Suppositories

Suppositoria Laboratories, 4718 18th Avenue, Brooklyn 4, N. Y., have issued a four-page folder listing their long list of suppositories for many conditions.

Custom Made Glassware

Corning Glass Works, Corning, N. Y. has issued a 124-page book entitled Custom Made Glassware by Corning. The book is a catalog of a wide range of laboratory glassware produced by the company.

1954 Accident Rates Booklets

National Safety Council, 425 North Michigan Avenue, Chicago 11, announces that the 1954 series of Accident Rates booklets is now available. The booklets contain the 1953 accident experience of companies that report to the Council, and are published annually for each of 15 industries.

Pallet Hand Lift Trucks

Yale & Towne Manufacturing Company, 11,000 Roosevelt Blvd., Philadelphia 15, has issued a 12-page brochure (P-673B) describing Yale Pallet Hand Lift Trucks. Profusely illustrated with actual application photographs showing how hand trucks can increase efficiency in handling a variety of materials, the brochure describes different pallet types and designs and gives their specifications.

Algin Gels

Kelco Company, 31 Nassau Street, New York 5, has issued a 4-page bulletin describing the use of their Algin Gels, giving formulas for many industrial uses.

Fatty Acids

A. Gross & Company, 295 Madison Ave., New York 17, has issued a new edition of Fatty Acids in Modern Industry. This 24-page booklet contains specifications, grades, packing, and Stock points on distilled stearic, oleic, coconut, cottonseed, soya, and palm fatty acids, as well as information on glycerine, pitch, and hydrogenated tallow fatty acids.

Dental Market Survey

Dental Survey Publications, Essex Building, Minneapolis 3, Minn., has issued a 36-page booklet entitled, A Survey of the Dental Market, which is described as a graphic presentation of valuable information on the 580 million dollar market. Research for the book started two years ago, and the figures presented are the latest available and are based on responses to a dental survey treatment study questionnaire covering 10,555 patients and how dentists treated them.

Organic Solvents and Chemicals

Chemical Solvents, 60 Park Place, Newark 2, N. J., have issued an 80-page booklet entitled Organic Solvents and Chemicals, giving complete information on a long list of solvents as well as additional information of use to users of solvents.

Bulletin on Indulin

A technical bulletin on the use of Indulin, a pine wood lignin for removal and recovery of proteins and enzymes has been issued by the Polychemicals Division of West Virginia Pulp and Paper Company, Charleston A, South Carolina.

New Colorimeter

An 8-page, profusely illustrated bulletin (FS-246), just published by Fisher Scientific Company, 717 Forbes Street, Pittsburgh 19, Pa., explains the theory and use of a new additive-colorimeter designed to serve as a permanent "color memory" for control chemists.

Pendit WA Cosmetic

Raymond Laboratories, 261 East Fifth, St. Paul 1, Minn., has issued an 8-page bulletin on Pendit WA Cosmetic, described as a brand of sodium lauryl sulfate.

Catalog of Personnel Material

Science Research Associates, Dept. XB, 57 West Grand Avenue, Chicago 10, is distributing the latest catalog of personnel material for business and industrial use. The catalog is said to be helpful in selecting better employees, increasing employee performance, choosing employees for promotion, and reducing employee turnover. Included are general personnel tests, as well as specialized tests for clerical and office, and shop and factory employees.

Where Volume and Reliability are demanded Stokes Tabletting Presses Serve

A few of the Stokes Model BB-2 tabletting machines in the modern plant of A. H. Robins Company, Inc., at Richmond, Va. These presses are of the rotary type, fully automatic in operation, with a production range of 750 to 1900 tablets per minute.

An industrial show place of the South is the new million-and-a-half dollar plant of A. H. Robins Company, Inc., at Richmond, Va.

This modern plant, handsomely landscaped and fully air-conditioned, occupies almost two acres of space on a single floor. The present annual multi-million dollar business is built on a line of 20 or more products developed from the single prescription item with which the business was started many years ago.

Typical of the modern equipment with which the Robins' plant is furnished is the battery of Stokes BB-2 automatic rotary presses for the preparation of tabletted products in numerous sizes and shapes.

Stokes tabletting presses are noted for the high production schedules which they help users to maintain while producing tablets of uniform size, weight, density and finish. Many Stokes presses have been in continuous service for 20 to 30 years or more.

Punches and dies for Stokes tabletting presses, including carbides suitable for exceptionally long runs or abrasive materials, are made in the Stokes plant. Send for the booklet "How to Save Money on Punches and Dies" and for Catalog No. 801, "Stokes Tabletting Presses."

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Management Forum

by Francis Chilson

INDUSTRIAL CONSULTANT

I Go in to See the Queen

Shortly after my arrival in London the early part of August, "Sir John" Walmsley asked me if I'd like an audience with the Queen. With something more than alacrity I said, "Sure!" So I put on my best bib and tucker, polished up my court etiquette and practiced bowing from the hips—a somewhat difficult feat in view of my stately paunch. Since "Sir John" knows everybody of importance in England, it never occurred to me to question the invitation. But the "Queen" turned out to be a barmaid in Soho who was a yard and a half across the bum and weighed about twenty stone—280 pounds. She sat in regal majesty, enthroned upon a bar stool, holding her scepter of authority—a bung starter.

This blunt, authoritative instrument has its origin in English history. Its prototype, the royal scepter, was originally a golden axe presented to Henry VIII. The King, being of a playful turn of mind, used the sharp edge to chop off the head of his Queen, Anne Boleyn, and, with the dull side, he bashed open the head of a barrel of beer to celebrate the occasion. The English took a very dim view of his playfulness, not because he had chopped off the Queen's head, a practice which is quite common in English history (and this explains why so many English pubs are called the "Queen's Head"), but because the Queen's blood was spilled all over the new, expensive Brussels carpet which was bought with taxpayer's money. The King could always get another Queen for little or nothing but who was to pay for a new carpet? (I may say in passing that the common English adjective "bloody" also has its origin in this little incident.) So to prevent any further waste of the taxpayer's money the English took the King's axe away from him and blunted the sharp edge, making it more or less club-shaped, the form it has today.

In keeping with tradition, as can be seen in Madame Tussauds, the English take a very dim view of doing away with your wife unless you beat her to death with a scepter-shaped club—which seems reasonable. If, however, you do the job with a cricket bat, the rules of cricket must be observed. The English are nothing if not sporting.

It is needless to say I was twitted endlessly about my "American accent" whatever that is. The English pride themselves on their ability to speak their own language flawlessly. But they have more dialects and accents than we do. We have but six: Bostonian, Yankee, Brooklynese, Southern, Western and a composite of all. The English have Lancaster, Yorkshire, Somerset, Cornish, Cockney, Oxford, Welsh, Scots, Dorset and several others. They also speak English—some of them. The only flawless English I ever heard was spoken by educated Dubliners. I reminded my English friends of this and I seized the occasion to point out that a substantial portion of classic English literature was written by Irishmen as well. When the row was raging, a bloke named Walters, who is the solicitor for Aspro Ltd., unintentionally ended the debate hilariously by saying, "I once knew a girl from Boston and you wouldn't have known she wasn't English, except for the fact that she rolled her r's." Ah me!

Sir John told me that in Stoke Poges church yard, hard by the stones that inspired Gray's Elegy, there is a moss-grown stone above the grave of a frustrated spinster which bears the inscription: "Who said 'you can't take it with you'?" English humor is so hard to understand.

In a single year England has gone through an amazing transformation. Everybody is working—unemployment being something less than one per cent, the irreducible minimum. The roads are jammed with cars. Ordinary folk who before the war never aspired to anything more pretentious than a motorcycle now are driving cars, old ones in many cases and very small ones in others, but cars nonetheless. And these people will never go back to pedal pushing or to motorbikes. Already the stimulating effect on England's economy is obvious. People do not aspire to those things which are far beyond their reach, but once they've had experience

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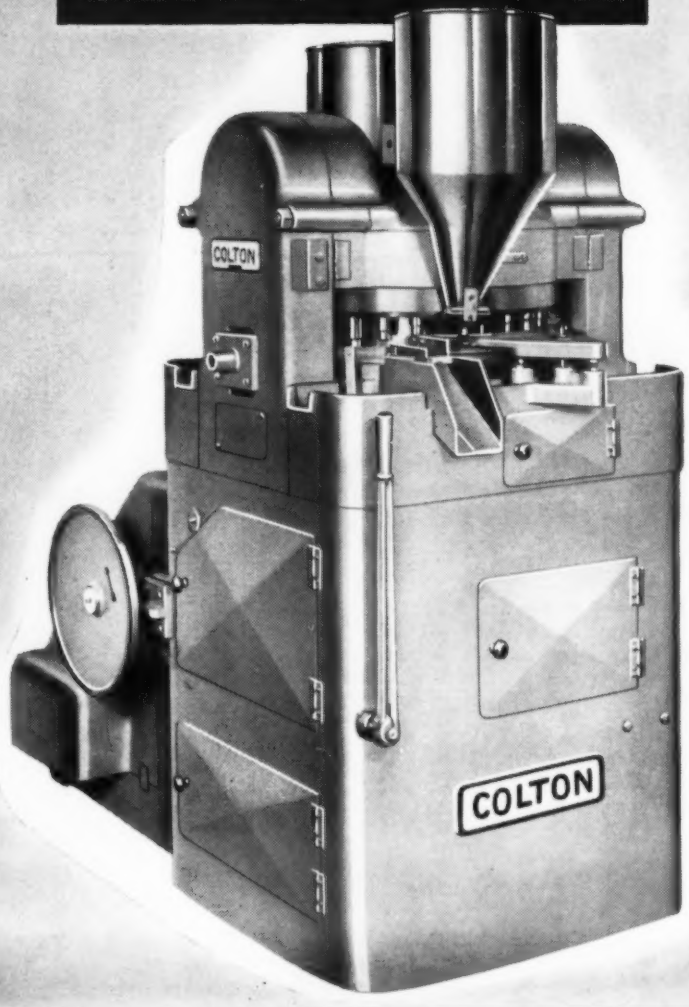
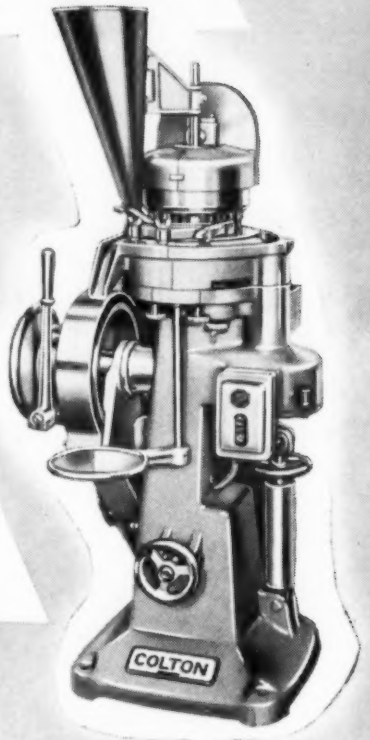


. . . world's fastest 16-punch single rotary tablet press . . . up to 1150 tablets per minute

Colton No. 216 Single Rotary Tablet Press (a best-seller when production was 800 tablets a minute) has been re-engineered and production stepped up to 1150 tablets a minute: sizes up to ⅝" diameter; ¾" depth of cell. Low first cost; low tool cost and quick, easy changeover to different products; variable speed drive; important NEW 3-Point Suspension Feed Frame for fast, precise adjustment and NO complex "front-to-back" weight adjustment. Performance equal to many antiquated, double (and expensive-to-tool) rotaries. Write for bulletin on No. 216.



. . . world's ruggedest high production double rotary tablet press . . . up to 2900 tablets per minute

Colton No. 260 Double Rotary Tablet Press is a high-speed, high-production giant so ruggedly built that it can be used for slugging as well as for tablet making. Pressures up to 20,000 lbs.; 25 to 41 punches; 1750 to 2900 tablets a minute; sizes up to 1 1/16" dia.; 1⅜" depth of cell; heavy duty motor; variable speed drive; anti-friction bearings; twin-disc clutch; automatic, adjustable excess pressure release; vital running parts dust-proof sealed; many other features. Write for bulletin on No. 260.

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of luxuries which formerly were the prerogatives of the rich and well-to-do, they will never go back to the modes of living they have discarded.

The cost of living is high in England, particularly for the working people, whose earnings ratio to cost of living is very much less than it is here. But that will be remedied in time. A way will be found to lower costs materially or wages will be increased all around. The productivity of the English workman has always been substantially less than ours through no fault of his own. He has suffered from poor industrial leadership and has been bound down by the caste system under which he could not voice his opinions freely because that was not "his station." This has been proved at Fawley where Esso Petroleum is erecting one of the largest oil refineries in the world. This project is being supervised by Americans but the work is being done by Englishmen. At the beginning of the project the productivity of English workers was far below American standards but in three months time the Englishmen were matching our productivity and doing it with a will. This project is the talk of all England and rightly so. Englishmen have proved to themselves that there is nothing sacred about time honored methods. They have seen that if a supervisor is properly trained he will be able to train others to work effectively and what is equally important he will be willing to listen to suggestions and advice from his men. This will be a bitter pill for English supervisors to swallow, trained as they were in a system which permitted an underling to speak only when spoken to. But they are learning to change their habits in management courses which have been established in many English universities.

The essential difference between the English and American point of view is that the English like things because they are old; we like them because they are new. Once the Englishman gets his head above the dusty rubble of the years we had better look to our laurels. The Englishman knows that in an increasingly competitive, increasingly industrialized world, his country cannot live long as a first class power unless he can produce better products at lower prices than his world-wide competitors. The Englishman knows that, unlike us or the Germans or the Russians, he must import all his raw materials and that to overcome this disadvantage he must produce with a degree of efficiency that has never been equalled—or go under. And he won't go under—mark that.

In a single year through the elimination of rationing English food and English cooking have improved to a marked degree. I even had Yorkshire pudding that didn't taste like a wet blanket as well as really superb steak and kidney pie. In the month's time I was there I didn't have a meal that I could criticize from the point of view of cooking or quality of food. Of course I didn't have time to get out of London and so cannot report on the hinterland.

The English theater is burgeoning as you can imagine from the names of the leading plays. As you walk down Shaftsbury Street the theater marquees display these plays:

"THE BOY FRIEND"
"WISH YOU WERE HERE"
"INTIMACY AT 8:30"
"AFTER THE BALL"
"WHEN BOTH ENDS MEET"
"RELATIONS ARE BEST APART"

English names and titles are descriptive and logical. The English F.B.I.—Scotland Yard—is so named because it is not in Scotland nor is it in a yard. Quite obvious.

I have always heard it said that if you walk down Villiers street toward Trafalgar Square at sundown (when there is any sun) you will see, if you look up at Lord Nelson upon his pedestal high above the Square, that he is thinking of Lady Hamilton. It is a fact. An obvious fact I should say.

Everywhere you go you see and hear signs of the Americanization of England. You will hear American slang used by British toffs. You will hear American jazz played by all the British dance bands. I asked Nicky Walmsley, aged six, to name the two greatest heroes of England. Without hesitation he said, "Lord Nelson and Hopalong Cassidy."

"Sir John" sends his best wishes to you all.

Controller

Ever since my article on this subject was published I have been praised by the people who have to do things other than to fiddle with a plethora of paper work and roundly damned—by the controllers of course. Therefore I think the following letter from an Australian controller will amuse you, particularly the sentence in the last paragraph which I have taken the liberty of italicizing. I never knew before that controllers might be the cause of industrial expansion since 1914. I thought they were an effect—a rather irritating effect I may say. Like boils. It is good to know that Aussie operating men suffer as we do. Misery likes company.

"For the first time in my 2 years' reading of your "Management Forum", I found interest shown by other sections of our management. In fact, by the time your magazine reached me, the book was folded open at the page containing your article, "Controllers," and it was more worn than the outside cover. The Sales Manager had commented; the Merchandise Director had commented; the Managing Director was in league with both. Typed copies are now available—in fact, I got March after I had read April magazine.

" I am forced to defend my race.

"WHY IS A CONTROLLER, A.....?

"Because he has no control. He has the thankless job of urging, advising, cajoling, people—who don't want change.

"The Production Manager has charge of his processing functions. The Controller reads the figures and by comparison shows the Production Manager where savings can be made, or production increased at the same

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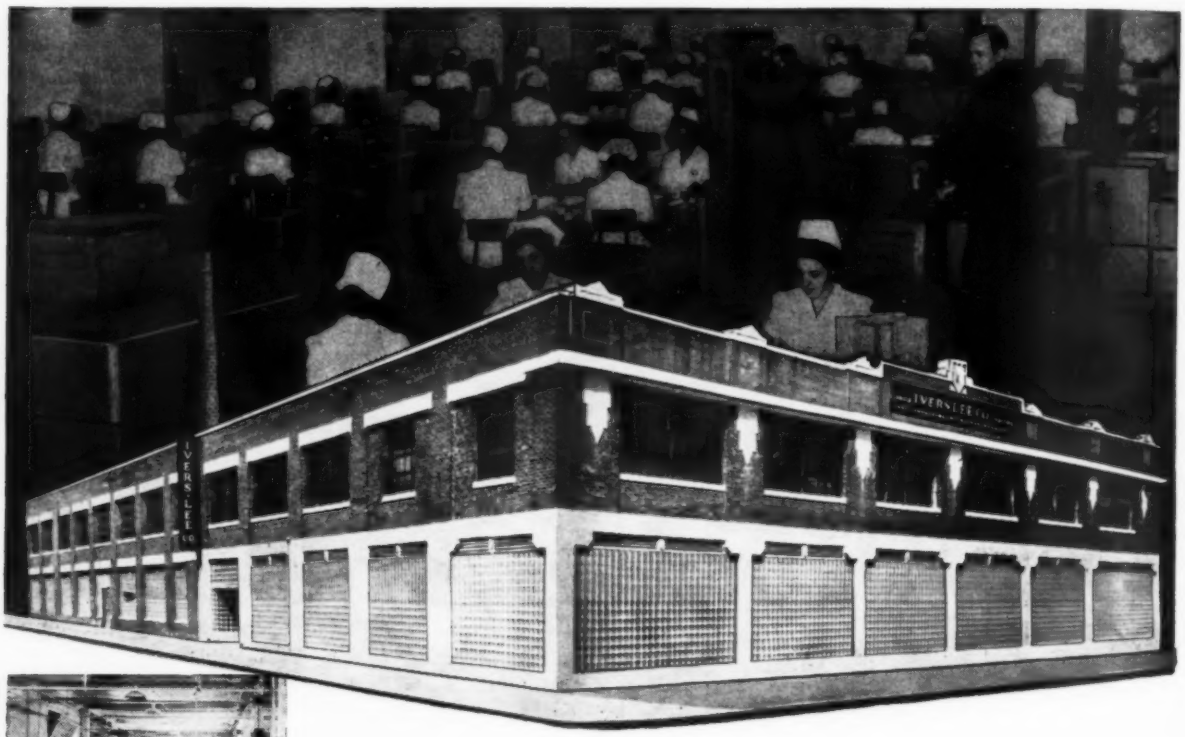

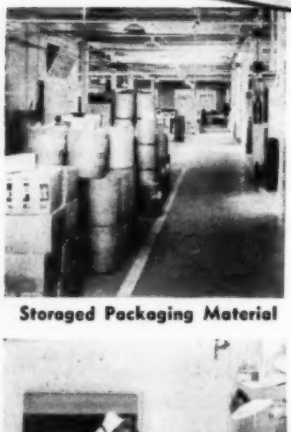

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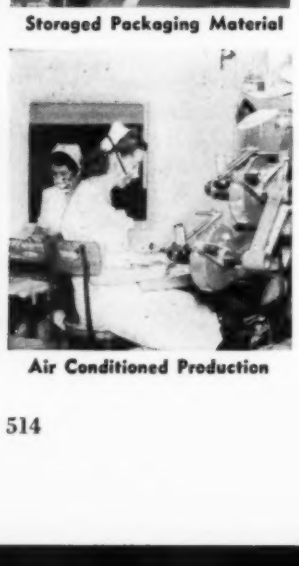

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Nowhere else but at I-L will you be able to obtain *complete* packaging services for such diversified products as tablets, creams, capsules and powders.

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Creators of a thousand and one different types of Unit-Packages for tablets, capsules, triturates, powders, creams and unusual products during 34 years of Packaging Service.

cost. Why does the Production Manager object to this man doing his job? As a progressive engineer he should welcome the opportunity to prove that he can do better even than the Controller thinks possible? Most Controllers would welcome the opportunity to try out their ideas themselves, or to work with people who would.

"The Sales Manager knows his selling business but he only knows how much he sells by reference to the figures produced by the Controller. The Controller can tell him whether what he sells is profitable; whether the type of car in use is economical; whether the trip, the distance is economical; whether he can afford to Discount certain Sales. But the Sales Manager doesn't trust the Controller, so he gets his men to estimate this and estimate that, duplicating work in an endeavour to prove that the other fellow is wrong. Why do people who don't deal in figures think that Accountants can't see beyond them?

"Fact is, figures show the effects—we want the cause.

"The Warehouse Manager has his schedules and difficulties to meet. His interests lie in service. The Controller can tell him (by using figures, comparing this section with that section, this method with that method) which is a better way to handle the goods—not only economically, but in practice. The Controller cannot put the scheme in use, but only advise, and why is that advice always frowned on and ignored as long as possible? Because he's not a "Warehouse" man and couldn't possibly know what was a better way!!

"I wonder why Controllers were ever thought of. Did management decide they required people to use the figures the Accounts Department were producing? Or is it that the men who are Controllers sold the idea to management? They must be good Salesmen for they are still there and they are necessary. *I wonder if it is through Controllers that industry has expanded to such an extent since 1914!* The number of people on the Office side increased with the increase in business and the increasingly urgent demands of business to give information sooner. The Tax Department is not excluded. And surprise of surprises: Offices are now mechanising and reducing staff!! Happy?"

Conventions

A few months ago I called attention to the economic waste of duplicated conventions and trade associations in this industry. I anticipated that article was approved by some people and roundly damned by others. (It was not to be expected that any of the trade association secretaries would be for it—although one of them did suggest the consolidation of the principal manufacturing associations. Being a trade association secretary is a profession, and, since there are about 75,000 trade associations in the US, there is of course an Association of Trade Association Secretaries. Presumably they have conventions too.) No one wants his job opportunities restricted.

My article did not condemn necessary associations or necessary conventions. It merely pointed out the waste in duplicated associations and conventions. In a recent discussion I made the assertion that conventions must cost the pharmaceutical industry not less than $15,000,000.00 annually. Dues paid trade associations are a mere drop in the bucket. The big cost consists of executive's time, traveling expenses and entertainment expenses.

I doubt if any firm in the trade has attempted to compute what attendance at conventions costs. Accounting being what it is, convention costs are not dumped into one account and re-distributed to divisions. Such expenses are charged out directly to the departments involved. Thus the marketing people's convention expenses are charged to sales expense; the chemists to research; the production people's to factory expense and so on. But nobody that I ever heard of charges to convention expense the cost of executives, time even though their time, especially when they are on committees, may run as much as ten or fifteen per cent of their total time. It would be interesting to make a detailed study to see if the costs always justify results.

That there are results from conventions no one can deny—good results and bad results. At conventions I have witnessed the beginning of mergers, I have seen deals initiated, I have seen useful information swapped, I have seen permanent friendships created where there had been enmity before—and I have seen the opposite too, more than once.

So what is the balance? Red or black?

The point I make is that while trade associations and conventions are necessary (although European businessmen seem to thrive without them) duplicated associations and conventions are not.

Some of the large firms especially among suppliers attend so many conventions and belong to so many trade associations that they have been forced to appoint certain officials to do nothing but attend conventions. It's a hell of a state of affairs—especially when you consider the fact that everybody is complaining about the dearth of executive talent. One V.P. told me he has to attend 20 conventions annually. Since he gets a month's vacation this means that almost exactly half his time is devoted to attendance at conventions since each convention kills a week. If the time he spends at committee meetings was added, it would be found that he spends more than half his time at conventions. Maybe it pays in such extreme cases but I doubt it.

As a management technique I think duplicated conventions are over-rated. Top executives complain all the time about the high pressure under which they work and then they attend a lot of high pressure conventions, where they play too much golf in too short a a space of time, where they stay up too late for too many nights in succession; where they drink too much—some of them—in too short a space of time. And then they wonder about the insurance statistics on fatalities due to heart disease—especially when one of their friends becomes an insurance statistic.

it takes a PRO TO SOLVE A LABELING PROBLEM!

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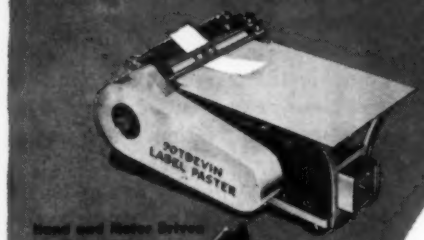
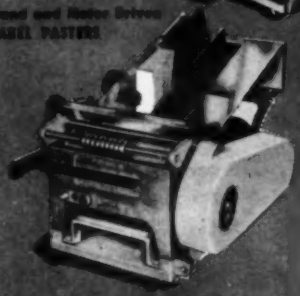


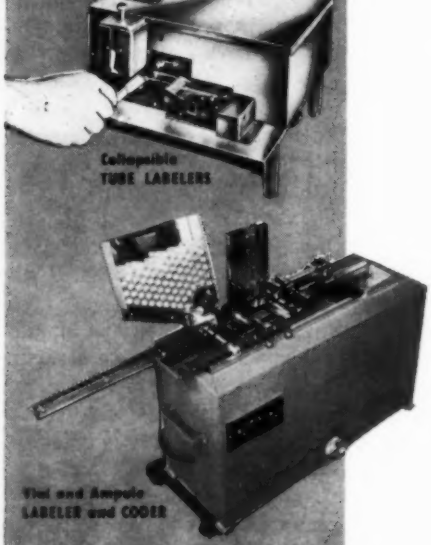
Hand and Motor Driven LABEL PASTERS



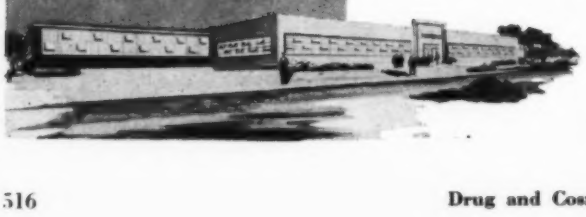
Semi-Automatic Feed LABEL PASTERS

LABEL ACTIVATORS for Thermoplastic Labels

Collapsible TUBE LABELERS



Vial and Ampule LABELER and CODER



Ideally suited for short-run production or for auxiliary use so as not to disturb a mass production set-up. Write for literature and details on **FREE TRIAL OFFER.**

Hand and Motor Driven LABEL PASTERS
Highly versatile, handles any shape label without adjustment. Dial control regulates paste flow, eliminating excess. Cuts stock loss. One machine can supply several operators. Available in 6"-8½" models.

Semi-Automatic Feed LABEL PASTERS
Quickly adjustable to all shapes of labels, from ½" to 7½" wide. Dial regulates paste flow. Speeds production up to 50%. Suitable as auxiliary unit in mass production operation. Leaves mass production equipment undisturbed.

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Activates delayed tack, pre-coated labels quickly and evenly. Permanent labeling on glass, metals, plastics, fabrics, etc. No water or glue to smear product. Thermostatic heating control. Small and portable. Available for 6" and 12" widths. Motor driven.

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Applies 32 slip labels per minute to collapsible tubes. Automatically forms and ejects label on tube. Machines for ⅛, ¼, ½, 1 oz. tubes.

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Thermoplastic labelers in 1, 2, 3, 5 and 10 c.c. sizes. Hopper automatically feeds vial or ampule for labeling and coding.

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Specializing in Labeling Machines for over 60 years

The Insurance Racket

The insurance companies in this country have used the "scare technique" to such advantage that they have American business men buffaloed and they have used the technique to such advantage that the insurance companies are the richest and most profitable—not to say powerful—of our financial institutions.

Speaking of fire insurance alone, the fire insurance companies are insisting upon a lot of ridiculous, uneconomic fire preventive measures ever since the General Motors fire.

In effect the insurance companies say to you, "Yes. We will insure you against fire loss. But you must adopt all the fire prevention devices and construction features we tell you to in order to prevent us from ever having to pay you a dime on a fire loss for which you are paying us substantial premiums."

If you do have a fire loss, they will welch out of paying you a nickel if there is the remotest chance that they can get away with it. If they find that your attorneys have read all the fine print on the policies before you have signed up and they can't get out of their obligations, they will pay up. Then they will rate you up to compensate for their loss or they may exercise their right to cancel your insurance altogether.

Insurance companies are not interested in your operating costs. If they had their way your plant would be broken up into a series of independent buildings and each building would be equipped not only with sprinklers but complete CO_2 systems as well. If you have a big open building they must have it chopped up with Class A firewalls equipped with Class A firedoors. Cost is no object so long as it is your money. Waste of space and interference with material handling is not their concern; it's yours. You've paid them plenty of money to protect you in case of fire loss and they want you to invest plenty more to keep them from having to pay.

Recently I had a hand in the construction of two new plants. In the first instance it was found that it would take 35 years to amortize the cost of the sprinklers and the separate water tank that the sprinklers required. (The insurance companies won't accept anything but an independent source of water.) So the management very wisely said, "To hell with it."

In the second instance the management fell for the insurance company's palaver, so we installed an unsightly, elevated water tank and a complete sprinkler system (in spite of the fact that all hazardous processing units are blanketed with an automatic CO_2 system) at a cost—not including maintenance—which will take us 30 years to recover in insurance savings.

Yet, if you went to the same management with a proposal in ordinary business matters that would take 30 years to equalize itself, you'd be tossed out on your ear. As a matter of fact this very same management told me that they would not consider the purchase of new equipment for production purposes unless I could demonstrate that it would pay off in two years. In reckoning the saving from production equipment they cut the apparent saving in half to absorb the corporation taxes of 57 per cent, on the ground that the only saving that counts is the saving that is left after Uncle Sam has had his cut.

Consistency is a virtue—or maybe I'm nuts.

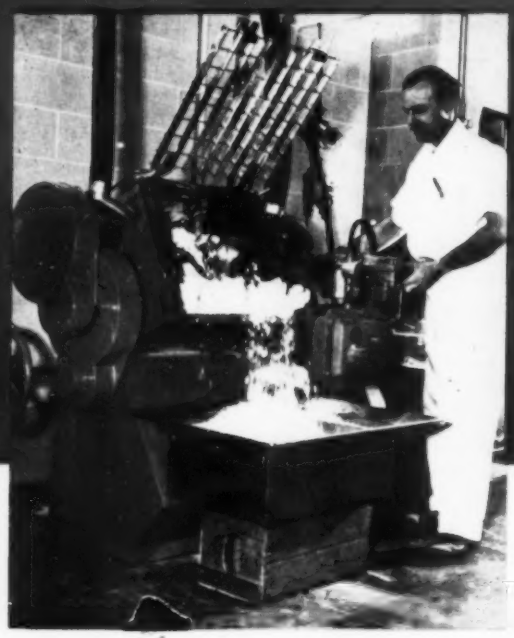
In England British business men cannot be moved by "scare techniques." Consequently they don't sprinkler their plants at all as a general rule. Only those plants are sprinklered that deal with highly inflammable material which can be extinguished with water. Plants dealing with highly inflammable solvents are protected by CO_2 systems. I am working on two large new plants over there now and neither is to be sprinklered. In England fire insurance premiums are the same whether the plants are sprinklered or not. Since it is the same insurance companies—or largely so—that operate on both sides of the water, it is an anomaly that what they can't get away with in England, they have been able to make us pay through the nose for here.

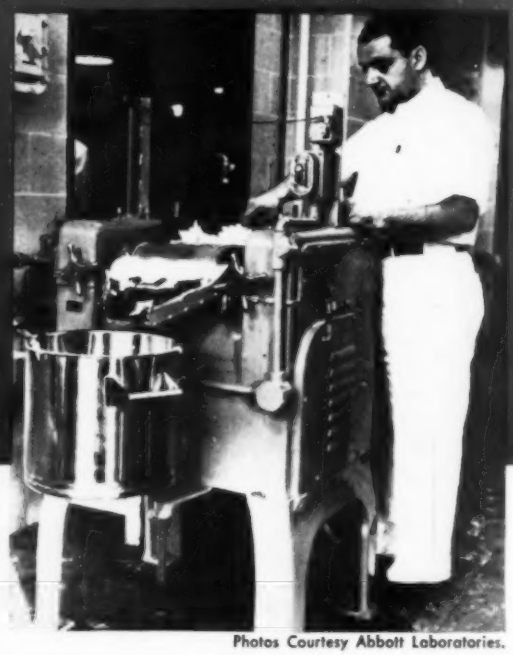
I am all for sensible fire precautions. (And good housekeeping and cleanliness throughout the plant are among the best of precautions.) But I don't believe in adopting precautions that are not only uneconomic but asinine. I remember once that I found a client's raw material inventories scattered in five different buildings dispersed over several city blocks. Thirty-five years before they had had a fire that destroyed their raw stocks. The stocks were replaced within a few weeks' time but upon the urging of the insurance people the stocks were dispersed in order to protect the insurance company. In the intervening 35 years the extra cost of handling those materials was several times greater than the original fire loss but nobody had noticed because such costs were buried in overhead. The stocks are consolidated now.

One thing you can be more certain of than payment of full fire damages by insurance companies: If you should be unfortunate enough to have a fire your suppliers will ignore their other customers and do their damndest to get you into production again. Recently a client had a fire loss from a solvent fire. The plant was not sprinklered—fortunately. If it had been the fire would not have been put out anyway, because you can't fight a solvent fire with water, but an immense amount of finished stock in the adjoining room would have been destroyed by water. In five minutes the local fire companies were on the job and kept the fire localized. The room in which the fire occurred was destroyed. What impressed me was the loyalty with which suppliers of material rallied around and worked overtime without extra charge to replace the ruined materials. Building material suppliers re-routed materials destined for other jobs in order to help us get started again.

The most serious damage a drug or cosmetic factory can suffer from fire is in the places where it is least likely to occur—in its packaging and processing departments. Especially the former, for with all the good will and special attention in the world, a machinery supplier cannot divert equipment fitted with special parts that will not fit your containers. That takes time. Raw in-

DAY EQUIPMENT SELECTED FOR PILOT PLANT, WHERE PRECISION IS VITAL!





Photos Courtesy Abbott Laboratories.

Efficient method for wet granulation is demonstrated in this picture of a Day Stainless Steel Kneading and Mixing Machine, used for combination powder and binder to manufacture medicinal tablets.

Used here for smoothing ointments, the Day 5 X 12 Lab Three Roll Mill demonstrates its excellent application for laboratory and experimental operations of all kinds.

Pilot operations set the pattern for full-scale production. That's why heavy emphasis is placed on efficiency and precision. Abbott Laboratories demonstrates the excellence of Day equipment by choosing the two machines illustrated here for use in its pilot plant.

DAY Kneading and Mixing Machines,

No. 18 and No. 24, with capacities of 15 and 30 gallons, are ideal for experimental production. They can be equipped with DAY double-arm-sigma or fishtail agitators, depending on the material to be processed. They feature a dependable gear drive and power dump. Tanks are furnished in plain or stainless steel and may be steam-jacketed if desired.

DAY Midget Three Roll Mills

offer all the advantages and design features of larger Day models in a size adaptable for pilot operations. An extra heavy frame houses the gearing and motor, minimizing space requirements. Silent chain drive eliminates friction loss ordinarily encountered with shafting and belting. The 5" by 12" mill, as illustrated, is equipped with chamber bored rolls for water cooling or steam heating, whichever is desired.

DAY

THE J. H. DAY COMPANY • CINCINNATI 22, OHIO
INCORPORATED

ventories can be replaced quickly. Finished stock can also be replaced quickly through the good offices of private label houses and your competitors as well. Everybody is willing to lend a hand to anyone who has had a disaster. Look how the automotive trades rallied around General Motors.

I am all for fire prevention. Immaculate housekeeping, cleanliness, good maintainence, alertness and carefulness in handling inflammable materials and rigid insistence on the "No Smoking" rule will do more to prevent fires than all the fire walls and do-dads that your insurance people insist upon.

The following information is supplied by manufacturers of the equipment described, and claims made below by these manufacturers are passed along for what they are worth. Presentation of such notice in this department is not to be taken as endorsement of the claims or of the equipment.

Mechanical Presses for Forming Powered Materials

Cleanliness of operation is the outstanding feature of these new presses, designed especially for pharmaceutical processing where contaminating dust, grease and oil must be kept out of tablets. Full enclosures around fly-wheels, pulleys, cams, gears etc. not only prevent contamination of the material being pressed, but eliminate entry of foreign particles into these parts of the machine. Moreover, they eliminate danger as to the operators and set up men.

These presses are built by Haller Inc., 68 Ann Arbor Road, Plymouth, Mich., in a range of sizes from eight to 40 tons. They are of rugged construction and contain an individual motor drive.

The main frames are cast and are mounted on welded bases. The bearings are full-length bronze sleeve type with easily accessible grease fittings. The press speeds may be selected through a cone pulley belt drive. In larger models, a two-speed gear reduction with a shift lever on the front control panel is added to the cone pulley drive. Safety guarding has been emphasized, and gates isolating the die and punches from the operator are interconnected with the clutch lever. This prevents the press tools from being put into motion when the access door is open.

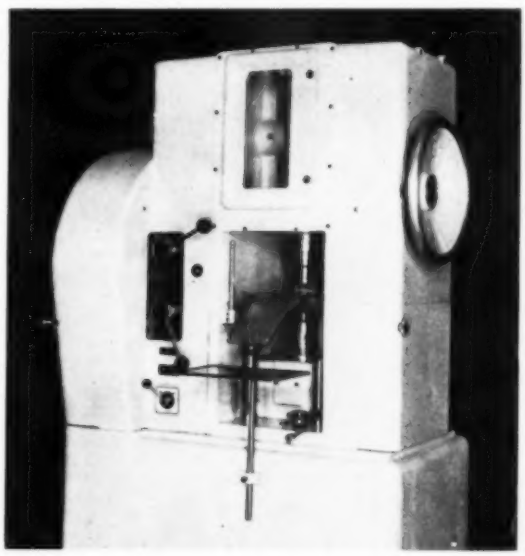
In the small and medium sizes the pressing motion is obtained from an eccentric which is adjustable from the front of the machine. A lock and reduction pinion, together with an engraved scale and indicator are provided for ease in adjusting the upper ram stroke to the precise requirements of the part being pressed. This adjustment, and the adjustment of the ejection mechanism, are made while the press is at rest. The settings are locked. The depth of fill or the weight of the part to be pressed may be adjusted while the press is in motion. This is done with a convenient hand-wheel or screw, located on the front of the machines. The ability to make this adjustment while the press is operating makes closer control of weight possible, saves material which would otherwise be rejected, and also saves production time. The press operator does not have to be skilled in tool set up to make this adjustment.

Powder is fed to the die cavities by an easily-removable shuttle type hopper, operating on the back of the die table. This feed has several features. It distributes the powder uniformly over a wide area, enabling the maximum die cavity to be uniformly filled. The feed shoe oscillates during the time it is over the die cavity. This movement, as well as the advance and retract, causes rotation of a small rake which serves to agitate the powder, remixing it to counteract any tendency for segregation of fines, bridging or packing. The lower punch fall is timed with the shaker shoe so that the retreating punch actually draws a change of powder into the die. Thus the feeding rate is seldom, if ever, the limiting part of the total pressing cycle. The feed shoe moves the finished parts forward over a chute into the finished parts container.

In smaller machines where the thickness of the part is limited, the pressure is from the top only. For thicker pieces the larger machines are equipped with a floating die table, which is controlled by specially-designed springs to produce the effect of lower punch pressure. Ejection is accomplished by the lower punch in the conventional manner.

Precision construction, ample provision for lubrication and short linkages enable these machines to run at high speeds. The straightforward design and the provision for taking up play in the principal slides assures new machine performance throughout the life of the press. Replacement parts are only required in case of accidental damage.

The machines are delivered with a full set of tools for proper maintenance. Spare parts are readily available. For assistance with special tooling and recommendations on specific problems, get in touch with Haller Inc.



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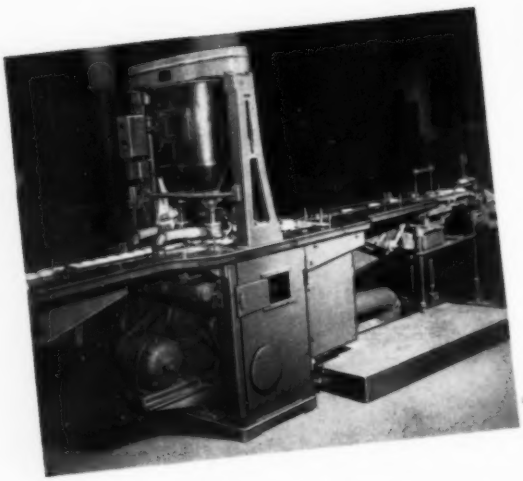

View of the S & S HG-84 Automatic Heavy Duty Duplex Filler at Avon Products, Incorporated, *Suffern, New York*

Whatever your product, profits begin with accurate filling. You can maintain this vital accuracy in your operations with S & S Filling equipment. There is an S & S Filler for most every product; paste, granular substance or powder. Prompt attention will be given to your request for complete information.

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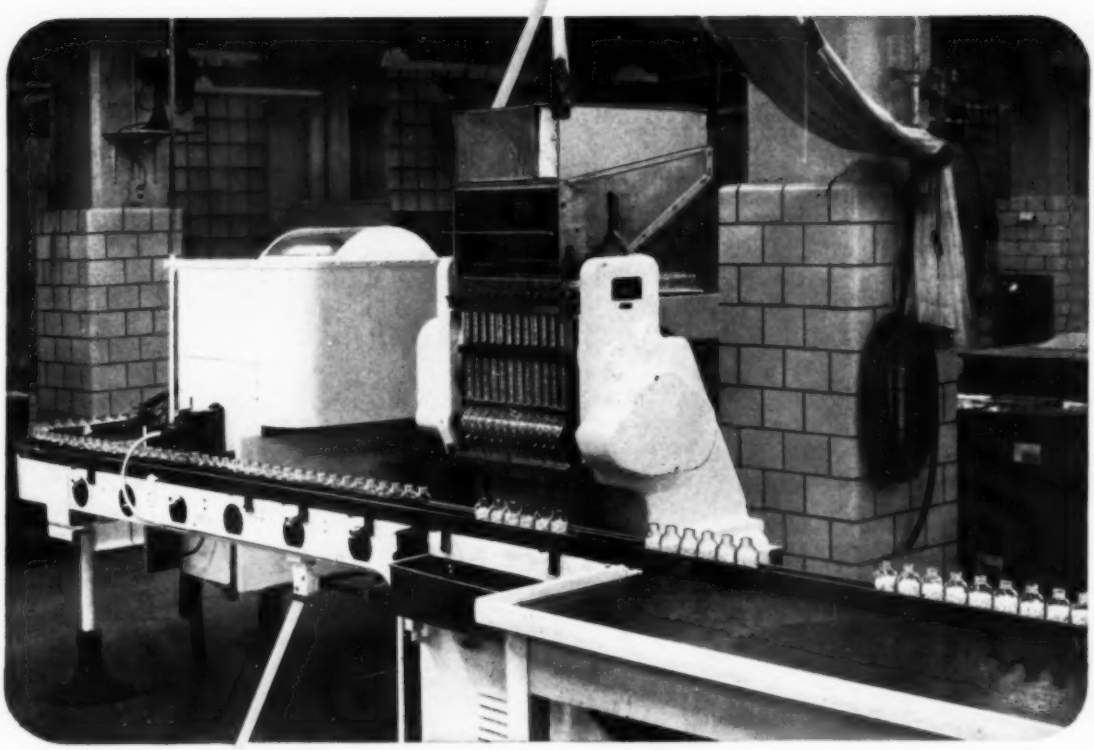

Model TBS Automatic Fills 160 Empirin 25-Tablet Bottles in a minute at Burroughs Wellcome!

Burroughs Wellcome & Co. of Tuckahoe, New York, uses several Model TBS Automatic Tablet Filling and Counting Machines to package their well-known Empirin Tablets. The company uses several bottle sizes—and finds that Model TBS machines are ideal for many operations because they are easy to change over for different counts and containers. The machines' specially designed tablet handling mechanism virtually eliminates breakage or powdering.

Model TBS Automatic Tablet Filling Machine in the 12 chute model will fill bottles, cartons or cans with any desired number of pills, capsules or tablets—counting and inserting them at rates of 160 per minute on 25 count or less,and up to 100 per minute on larger count containers.

Model TBS machines are available with many modifications to suit either mass production packaging of a single pharmaceutical tablet or speed packaging of a varied line of products. For complete details, write **US.**

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Elgin EARNS ITS WAY

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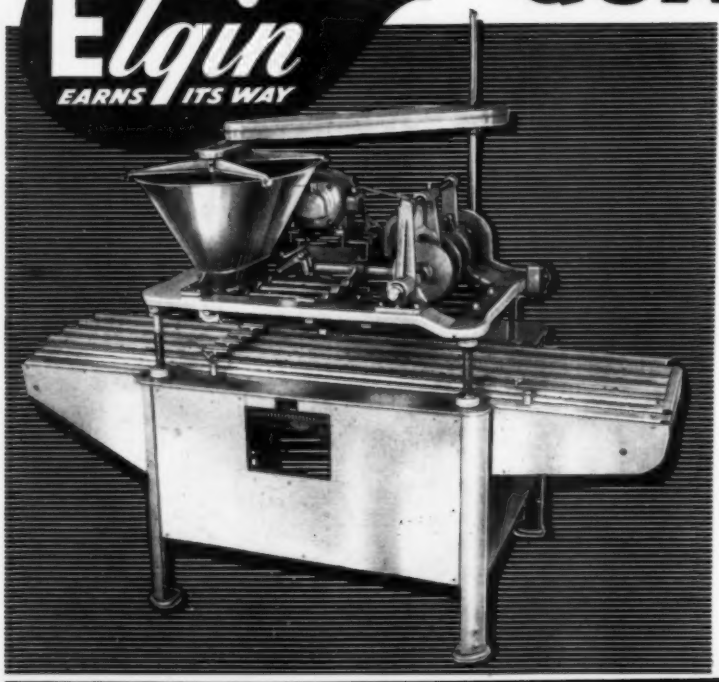

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NEW Bulk Label-Coder Imprints 5* Legends in 1 Impression

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New Model "C" CORLISS-CODER

- Fully automatic ... self-stopping
- Adjusts for die-cut or rectangular labels from 1"x¾" to 5½"x3"
- Delivers imprinted labels in perfect stack
- Foolproof ... cannot "skip" or jam
- Maximum production at lowest cost

Now, with this new Model "C" CORLISS-CODER, you can imprint code, expiration date, lot number, size, quantity, flavor and other changeable legends in a single bulk run... automatically. This compact bench machine handles a full hour's capacity of labels without requiring operator attention... affords extremely clean, sharp imprints consistently... takes only 10-minutes for changeover to different label sizes, less for copy changes.

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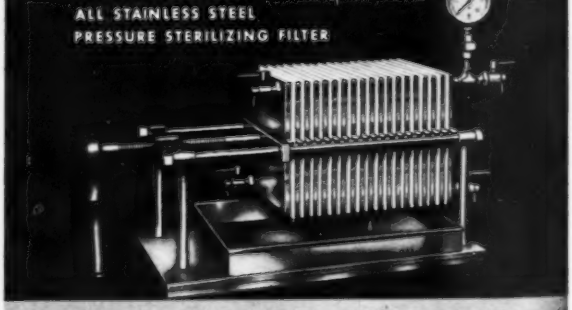

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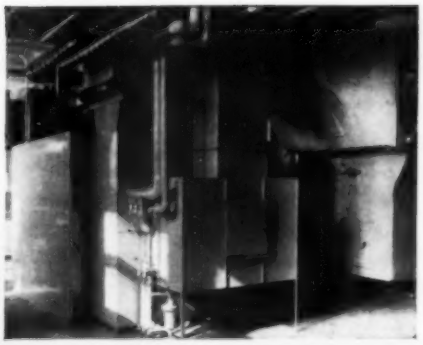
Lectrodryers serve low humidity areas in Pfizer plants all over the world



This air-conditioning type Lectrodryer maintains a constant 10% relative humidity in the antibiotic filtration room at the Groton, Connecticut, plant of Chas. Pfizer & Co., Inc.

Keeping relative humidity as low as 10%

The battle against contamination may be lost if control of vaporous moisture is not pinned down. Your best weapon is a Lectrodryer*. It can maintain bone-dry conditions in a room, over a process, throughout a laboratory and in air or gas lines . . . without disturbing required sterility. It reduces moisture to a harmless level below the point where hygroscopic materials would be affected or their flow interrupted.

Lectrodryers are helping to protect Pfizer quality in the United States, England, Belgium, Spain, Japan and South America.

Lectrodryers use Activated Aluminas to adsorb moisture from air, other gases and organic liquids. They efficiently reduce dewpoints to below −100°F . . . reduce relative humidity to as low as 5%. They can work under pressures as high as 6000 psi. Maintenance is minimized because these machines have few moving parts and Activated Aluminas will not wear out.

Perhaps you can benefit by reading Lectrodryer literature or talking with Lectrodryer engineers. Write for *Because Moisture Isn't Pink*, a booklet describing how industries are using Lectrodryers. Request any DRYness engineering information. Pittsburgh Lectrodryer Corporation, 309 32nd Street, Pittsburgh 30, Pennsylvania.

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Use this Schimmel specialty instead of
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Advancing Therapy

Chlorpromazine in Alcoholism

It is pointed out by J. F. Cummins and D. G. Friend (*Am. J. Med. Sci.* 227: 561, 1954) that one of the pressing problems in the treatment of any alcoholic is the adequate control of the withdrawal symptoms of tremulousness, excitement, and agitation accompanying any present day therapy. In utilizing disulfram therapy, it is necessary that the patient be without alcohol for a period of six days prior to the initial administration of this drug, if a disulfram reaction is to be avoided. This period of sobriety has been a hazard for many of those embarking upon the disulfram program because no medication previously available would control the psychomotor agitations as effectively as "one more drink." However, during the past year, Cummins and Friend have studied the action of chlorpromazine (Thorazine) and found it to be effective in preventing nausea and vomiting produced by a wide variety of drugs and clinical conditions. Since it is well known that nausea and vomiting are commonly produced by the ingestion of disulfram in the presence of alcohol, they decided to evaluate the effectiveness of chlorpromazine in suppressing these symptoms. In addition to its antiemetic effect, it has been observed that this compound also exhibited a mild sedative effect. It was felt that this feature might prove somewhat useful in reducing the psychomotor excitement.

As a result of these studies, Cummins and Friend developed a method for treating chronic alcoholics which eliminates the need to wait for "drying out" prior to the administration of disulfram. They found that disulfram and chlorpromazine, when administered together in adequate dosage to the inebriated alcoholic, produces a tranquilized state more effectively than with any current method of sedation. No untoward side effects have been noted in the treatment of 60 alcoholic patients. Nausea, vomiting, and hypotensive episodes have not been noted with this combination of drugs. Chronic alcoholics treated in the described manner do not suffer with the usual post-alcoholic psychomotor agitation.

Potassium Perchlorate for Hyperthyroidism

In their preliminary paper A. F. Godley and J. B. Stanbury (*J. Clin. Endocrin. & Metab.* 14:70, 1954) report that potassium perchlorate has been used in the treatment of 24 patients with Graves' disease. Oral administration of 200 to 400 milligrams every eight hours was effective in controlling the disease, as demonstrated by symptomatic improvement of the patient and a return to normal of the basal metabolic rate and serum concentration of protein-bound iodine. Thirteen patients had subsequent subtotal thyroidectomies. Two patients are euthyroid and have stopped treatment, and the remainder are either being treated continuously or have had their treatment interrupted. Preoperative addition of potassium iodide to the perchlorate caused an escape from control of the thyrotoxicosis in several patients. Two reactions which possibly were toxic manifestations of potassium perchlorate involved the gastrointestinal tract.

In the opinion of Godley and Stanbury potassium perchlorate is an effective antithyroid agent in the preoperative or continuous treatment of thyrotoxicosis. It is of particular value in those patients who are sensitive to, or fail to respond to the drugs of the thiourea group or iodide. Further experience and study are required for full evaluation of this new antithyroid drug.

Vitamin B_{12} for Psoriasis

That large doses of vitamin B_{12} may be of value in the treatment of psoriasis is indicated in the preliminary clinical report by R. Ruedeman, Jr. (*Arch. Dermat. & Syph.* 69:738, 1954). He found that 1 cc. of a 1,000 microgram dose given intramuscularly daily for 10 days consecutively, followed by a maintenance dose, gave best results, and in severe cases daily doses were carried on for 15 to 20 days or longer, consecutively. In some refractory cases, no results were noted until 20 or more injections were given. Experience will eventually point out the best routine. No reactions, local or general, were encountered, but marked improvement as to well-being, with more zest to carry on, was observed by all the patients. There were 34 patients—14 male, 20 female—ranging from 21 to 68 years of age. The duration of the disease varied from 7 months to 38 years. In 11 patients, the eruption involuted. Ten patients showed 75 to 85 per cent improvement, while six patients are slowly improving and treatment is continuing. Two noncooperative patients showed no results. There was slight recurrence in five patients. In these cases, treatment had been stopped too soon, but was resumed with good results.

Ruedemann feels that treatment with high doses of vitamin B_{12}—1,000 micrograms per cubic centimeter, intramuscularly — has surpassed all previous methods in rapidity of results; lack of reactions, ease of administration, stimulating cooperation, and bolstering the well-being of the patient. The rapid response of patients with long-standing recalcitrant psoriasis would be difficult to attribute to spontaneous involution.

Drug Therapy of Hypertension

In discussing the value of drug therapy in the management of hypertension, C. Levy (*Delaware Med. J.* 26:36, 1954) emphasizes that thorough knowledge of the mode of action and of the side-effects of the various drugs that have been recommended for hypertension are necessary to properly understand the place of these drugs in the medical armamentarium. Before treatment is instituted, a thorough study of the patient must be made to ascertain the etiology of the hypertension. Since many patients with hypertension are asymptomatic and remain free of serious damage to vital organs for many years, the question of when to institute active treatment is difficult to answer. Levy discusses the hexamethonium drugs, the ergot alkaloids, the hydralazines, dibenamine, the vasodilators, the veratrum group of drugs, low salt diet, the thiocyanates, and the rauwolfia extracts. Before any of these agents are used, not only their advantages and disadvantages must be weighed, but a close

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supervision must be maintained as each patient may react differently. Hospitalization for study prior to use of these drugs is advisable. The effect of stressful situations and emotional conflicts cannot be overemphasized. Therapy should be withheld from patients with serious coronary atherosclerosis or brain or kidney disease due to the danger of vascular thrombosis when the blood pressure has been lowered. At times combinations of drugs may be advisable, utilizing the favorable effects of certain agents as (1) the renal vasodilatation of hydralazine (Apresoline); (2) the bradycardia of veratrum; (3) the sedative action of rauwolfia. While drug therapy is a step forward in the management of hypertension, its ultimate value will require the test of time.

Acetylcholine Injections in Neuroses

R. M. Phillips and J. T. Hutchinson (*Brit. Med. J.* 1:1468, 1954) have found that intravenous acetylcholine may be of benefit in the treatment of varied forms of neurosis. Crystalline acetylcholine chloride was used in their study. It was freshly prepared as a 10 per cent solution in distilled water, usually as 200 mg. in 2 ml. The patients were given the injection intravenously, at least one hour after a meal, and initially a dose of 50 mg. was injected very slowly to test the sensitivity of the patient. This initial dose was then generally increased during subsequent treatments by 50 mg. to the total amount of 200 mg. A reaction usually occurred after the rapid injection of 50 mg. of acetylcholine chloride, but the remainder of the 200 mg. could then be given more slowly to prolong the reaction. Extra care has to be taken in those very sensitive to doses as small as 25 mg. There was little in the way of after-effects, and most patients were able to leave hospital five minutes after the injection, although the more elderly benefited from resting for 20 to 30 minutes afterwards.

From studies on 211 subjects it was observed that the patients who were helped most fell within a specialized group of obsessive or obsessional tension states, which have been defined. Of 104 patients in this group, 70.2 per cent were improved by the treatment. It has also been found useful in certain patients as a treatment complementary to E.C.T., modified insulin, and the emetine aversion treatment for alcoholism.

Over 6,000 intravenous injections of acetylcholine have so far been given. The treatment given with suitable precautions, has been found to be a safe one, and is relatively simple to use on an out-patient basis.

Isoniazid for Pleurisy

A. Carini (*Riforma med.* 68:148, 1954, through *J.A.M.A.* 155:865, 1954) used isoniazid to treat 19 patients with exudative pleurisy. The condition was the first clinical manifestation of tuberculous disease in 17 patients and secondary to a specific pulmonary lesion in two. Good effects were obtained in three patients in whom the elevated temperature and erythrocyte sedimentation rate dropped rapidly, the general condition improved, and the exudate diminished progressively leading to a complete recovery in about 20 days. The temperature, general condition, and erythrocyte sedimentation rate were benefited in 11 patients, but in these the pleural exudate remained unchanged, and a definitive recovery was obtained only with thoracentesis and injection of air. The general and pulmonary conditions were not influenced in the other five patients who recovered only after thoracentesis was performed and air introduced. According to Carini, isoniazid, although not the drug of choice for treatment of exudative pleurisy, is more useful than streptomycin, especially if it is used when thoracentesis is performed and air is introduced. This combined treatment not only causes the exudate to disappear but also prevents the onset of pleural adhesions with harmful effects on the respiratory function and, when the pleurisy involves the right side, on the cardiovascular function. Better results can be obtained in treating exudative pleurisy with this method than with administration of streptomycin alone.

Anisomycin: New Anti-Protozoan Antibiotic

B. A. Sobin and F. W. Tanner, Jr. (*J. Am. Chem. Soc.* 76:4053, 1954) report that a new monobasic antibiotic, anisomycin, has been isolated from two different species of *Streptomyces* and found to exhibit a high degree of activity *in vitro* against *Trichomonas vaginalis* and *Endamoeba histolytica*. The identity of the two preparations was established by a comparison of the infrared and ultraviolet spectra, elementary analyses, and mixed melting point. Crystalline anisomycin can be stored for long periods of time with no loss of potency. Aqueous solutions are quite stable over a wide *p*H range at room temperature. The compound can be distilled *in vacuo* a few degrees above its melting point. At the present time studies are under way investigating the efficacy of anisomycin in systemic *Trichomonas* infections in mice and *Endamoeba histolytica* infestation in guinea pigs.

New Cough Suppressant

In the study made by N. Ralph (*Am. J. Med. Sci.* 227:297, 1954) Dextromethorphan (dextro-3-methoxy-N-methylmorphinan hydrobromide), a new antitussive agent, was administered to 183 patients, of whom 39 were not included in the appraisal of the drug's merits as a cough depressant. Twenty-seven of this latter group had no cough and were given the drug solely for the purpose of determining its toxicity on prolonged administration. Of the 144 patients in whom the antitussive effectiveness of Dextromethorphan was studied, 107 had pulmonary tuberculosis, 22 bronchitis, eight bronchiectasis, four bronchial asthma, two lung abscess, and one bronchogenic carcinoma. Twenty-three patients (15.9 per cent) had slight to no relief of cough, 67 (46.5 per cent) derived moderate relief, and 54 (37.5 per cent) had pronounced to complete relief of cough. Better results were obtained with single doses of 15 mg. four times a day than with doses of four mg. also given four times a day. Hemograms did not show any untoward effect on the hematopoietic system. Similarly, these chronic toxicity trials failed to reveal any other side-effects, particularly on renal function, respiration, or blood pressure. There was no evidence of development of tolerance or addiction in these 23 patients or in any of the patients who received Dextromethorphan as a cough suppressant for as long as six months. Of the 183 patients treated with Dextromethorphan, use of the drug had to be discontinued because of nausea, vomiting and dizziness in only one patient. In addition, there was dizziness in one patient receiving a daily dose of 60 mg., but 30 mg. was tolerated without this sequela. Thus side-effects from Dextromethorphan were very rare. Dextromethorphan is a very effective and safe cough-suppressing agent having the antitussive activity of codeine without sharing its addictive properties and without producing the side-effects typical of codeine.

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Sun Screens

In commenting on the potential uses of sunscreening materials in industry (e.g. in plastics, autowaxes, protective wrappings, insecticides, etc.) it is stated in *Industrial and Engineering Chemistry* (46:15A, July, 1954) that the first and most important use for sunscreens has been in sunburn lotions and preventives. It is pointed out that sunburn radiation extends from about 2900 A. to about 3200 A., the shortest sun rays that penetrate our atmosphere. Peak burning activity has been variously located at 2967 and 3080 A. Rays between 3200 and 3900 A. promote oxidation of existing melanin to a darker material, but do not result in any significant burning. Thus, a compound that absorbs ultraviolet radiation in the 2900 to 3260 A. range, but transmits other light in the longer ultraviolet region will prevent sunburn but allow tanning. There is really no sharp differentiation between the burning and tanning ranges, but there is an area where tanning is adequate and burning is at a minimum.

Many different classes of organic compounds are able to absorb UV of various wave lengths, to a greater or lesser degree. Dypnone, piperonyl butoxide, umbelliferone, β-methyl-umbelliferone, aesculin, quinine salts, coumarin, digalloyl trioleate, pyrones, and derivatives of salicylic, anthranilic, *p*-aminobenzoic, cinnamic, and *o*-vanillic acids are among the more common sunscreens. French researchers recently announced several new highly efficient sunscreens — 4,5 - diphenyl - 2(3H) - imidazolone, disodium salt of 4,5-bis (*p*-sulfophenyl)-2(3H)-imidazolone, 4,5-diphenyl-2-mercaptoimidazole, isobutyl-*p*-dimethylaminobenzoate. Not all sunscreens are suitable for inclusion in a formulation which might be applied to a large percentage of total skin area several times daily. Dypnone (phenyl α-methylstyryl ketone), for instance, has excellent absorption characteristics. A coating of this compound only 0.000004 inch in effective thickness transmits less than one half of incident ultraviolet light. However, it stings the skin of some people, especially when wet, and so is not suited for cosmetic applications.

Special care must be used when selecting sunscreen agents for sunburn prevention. The material may be applied to a skin already damaged and sensitized by sun or wind burn. It will be used by persons of all ages, types of skin, and degrees of health. The material should not itself be subject to chemical change from sunlight, or from other agencies such as water or salts in perspiration. It should stay on for a reasonable length of time, and so should not be water-soluble. Thus, sunburn preparations made for the Army may contain glyceryl mono - *p* - aminobenzoate, 2-ethylhexyl salicylate, digalloyl trioleate, homomenthyl salicylate, or dipropylene glycol salicylate, in a hydrocarbon vehicle. Armed Forces specifications are that a preparation shall not transmit more than 1.0 per cent of the rays in the sunburn region through a film 0.001 inch thick.

New British Calamine Lotion

In developing an improved formulation for calamine lotion. D. Etchells (*Pharm. J.* 172:372, 1954) obtained results which suggest that a preparation containing the wetting agent, di - isopropyl - naphthalene - sulfonate, and carboxymethylcellulose as a suspending agent has advantages over the present and past lotions. The experimental lotion, the formula of which is given below, is of a thin cream-like consistency and is easily re-dispersed after storage by shaking. On application it spreads easily, dries fairly rapidly and leaves a fine film which is well retained.

Calamine, in fine powder	**15.00 parts**
Zinc oxide, in fine powder	**5.00 "**
Sodium carboxy-methylcellulose	**1.00 part**
Di-isopropyl-naphthalene sulfonate	**0.05 "**
Glycerine	**5.00 parts**
Liquefied phenol	**0.50 part**
Distilled water, to make	**100.00 parts**

The carboxymethylcellulose is best dispersed in about 60 parts of distilled water at about 70° C., with constant stirring. The lotion can then be prepared in the usual manner, incorporating the wetting agent with the powders and using the solution of suspending agent as the vehicle.

Etchells observes that the inclusion of a wetting agent decidedly increases suspensibility, and, although no great differences were observed in final particle sizes after storage, when lotions with and without the wetting agent were compared the number of larger particles was considerably less in the former than in the latter. The preparation described was compatible with most of the added medicaments, and, after storage, was readily re-dispersed. The inclusion of sodium carboxymethylcellulose had a two-fold purpose: to suspend the insoluble powders and to produce a fine adhesive film on application.

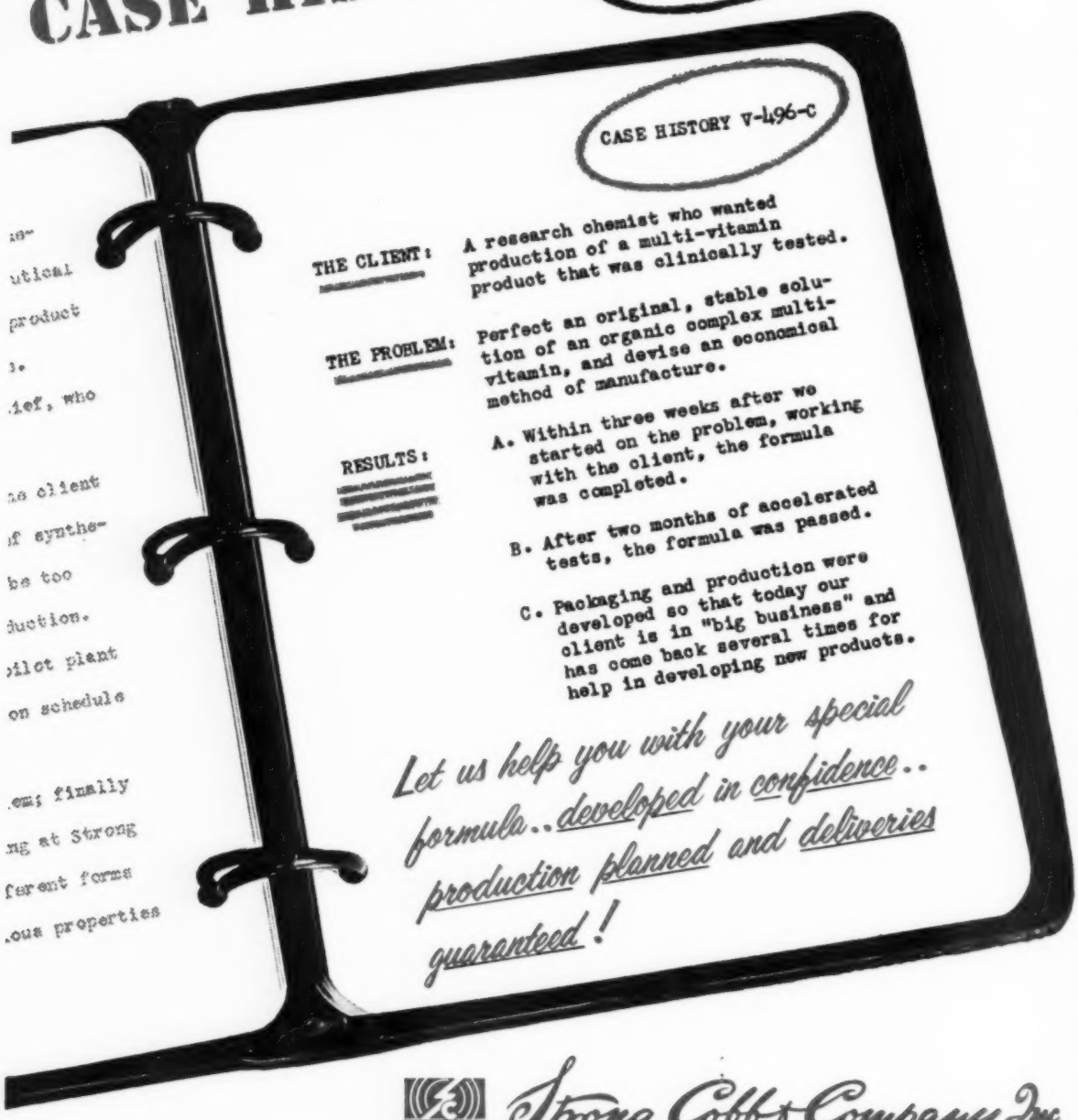
Benzalkonium Chloride in Eye Medication

The investigations made by J. A. Scigliano and M. W. Skolaut (*Bull. Am. Soc. Hosp. Pharm.* 11:37, 1954) were specifically aimed at the preparation of ophthalmic solutions that would be relatively free of bacterial growth. Their study showed that benzalkonium chloride is capable of freeing ophthalmic solutions of micro-organisms in a short period of time and maintaining this condition from time of compounding to the expiration date. The use of benzalkonium chloride 1:10,000 in solutions intended to be instilled in the eye appeared to be adequate.

On the basis of these findings, Scigliano and Skolaut recommend the following formulas for preparing ophthalmic medications:

1. Eucatropine hydrochloride	**1.00 Gm.**
Benzalkonium chloride solution 1:10,000, to make	**100.00 cc.**
2. Eucatropine hydrochloride	**1.00 Gm.**

CASE HISTORY V-496-C


CASE HISTORY V-496-C
THE CLIENT: A research chemist who wanted production of a multi-vitamin product that was clinically tested.
THE PROBLEM: Perfect an original, stable solution of an organic complex multi-vitamin, and devise an economical method of manufacture.
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Sodium phosphate, monobasic, anhydrous	0.40 Gm.
Sodium phosphate, dibasic, anhydrous	0.47 Gm.
Benzalkonium chloride solution 1:10,000, to make	100.00 cc.

3. Cocaine hydrochloride... 0.50 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

4. Pilocarpine hydrochloride... 2.00 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

5. Pilocarpine hydrochloride... 2.00 Gm.

Sodium phosphate, monobasic, anhydrous	0.40 Gm.
Sodium phosphate, dibasic, anhydrous	0.47 Gm.
Sodium chloride	0.26 Gm.
Benzalkonium chloride solution 1:10,000, to make	100.00 cc.

6. Atropine sulfate... 2.00 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

7. Tetracaine hydrochloride... 0.50 Gm.

Potassium phosphate, monobasic, anhydrous	0.43 Gm.
Sodium phosphate, dibasic, anhydrous	0.57 Gm.
Sodium chloride	0.34 Gm.
Distilled water, to make	100.00 cc.

8. Tetracine hydrochloride... 0.50 Gm.
Distilled water, to make... 100.00 cc.

9. Scopolamine hydrobromide... 0.25 Gm.

Potassium phosphate, monobasic, anhydrous	0.19 Gm.
Sodium phosphate, dibasic, anhydrous	0.81 Gm.
Sodium chloride	0.33 Gm.
Benzalkonium chloride solution 1:10,000, to make	100.00 cc.

10. Scopolamine hydrobromide... 0.25 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

11. Eserine sulfate... 0.25 Gm.
Sodium bisulphite 0.10 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

12. Homatropine hydrobromide... 2.00 Gm.
Benzalkonium chloride solution 1:10,000, to make 100.00 cc.

13. Homatropine hydrobromide... 2.00 Gm.

Sodium phosphate, monobasic, anhydrous	0.40 Gm.
Sodium phosphate, dibasic, anhydrous	0.47 Gm.
Sodium chloride	0.10 Gm.
Benzalkonium chloride solution 1:10,000, to make	100.00 cc.

Preparations for the Scalp

In his discussion of the management of dandruff and baldness, I. I. Lubowe (*Soap, Perf. & Cosmetics* 27:621, 1954) stresses that, in treating seborrheic dermatitis of the dry type, a shampoo should precede the application of the prescribed ointment to the hair and scalp. Various types of shampoos have been utilized, the most popular including: tincture of green soap, tar shampoo, castile olive oil shampoo, and soapless detergent shampoo. Tincture of green soap is antiseptic and cleansing. However, because of the excessive amount of alcohol it contains, frequently the scalp and hair become quite dry following its constant use. This can be avoided by application of heated olive oil rubbed into the scalp with the fingertips by moderate massage, following the shampoo. Tar shampoo is utilized when a stimulating and cleansing shampoo is desired.

Probably the most popular type of shampoo is the castile olive oil shampoo which contains a coconut oil soap, with a small quantity of olive oil soap to improve emolliency. The average scalp is cleansed excellently with the above type shampoo, and no cases of sensitivity have been reported in those cases where sensitivity to soap exists.

Soapless detergent shampoos, though excellent cleansing agents, occasionally leave the hair and scalp dry. The use of soapless detergent shampoo may be followed by massaging of the scalp with olive oil.

To the above and other shampoos Lubowe has been adding hexachlorophene, two per cent, as an antibacterial agent and deodorant. The inclusion of soluble lanolin products has been suggested and found to be of probable cosmetic value.

Lubowe cites the following as examples of popular antiseborrheic remedies:

1

Salicylic acid	1.8 parts
Precipitated sulfur	3.0 "
Hydrophilic ointment, U.S.P., to make	60.0 "

2

Salicylic acid	1.8 parts
Ammoniated mercury	3.0 "
Hydrophilic ointment, U.S.P., to make	60.0 "

3

Precipitated sulfur	3.0 parts
Bacitracin-Neomycin ointment, to make	60.0 "

Also useful is the following "Topotar" ointment:

Coal tar solution	5.0 Gm.
Colloidal sulfur	2.5 Gm.
Salicylic acid	3.0 Gm.
Zinc oxide	5.0 Gm.
Hydrophilic ointment, modified, to make	100.0 Gm.

For anti-pruritic effect, one-half per cent menthol can be added to the above basic prescriptions.

In considering the treatment of alopecia (baldness) of the scalp, Lubowe notes that the following is a frequently prescribed lotion for oily scalp:

Euresol	2.0 parts
Salicylic acid	2.0 "
Glycerine	6.0 "
Diluted alcohol, to make	120.0 "

Another scalp lotion, containing quinine hydrochloride, is prepared from:

Quinine hydrochloride	1.0 part
Tincture of capsicum	2.0 parts
Tincture of cantharides	6.0 "
Glycerine	6.0 "
Alcohol	32.0 "
Water, to make	100.0 "

Animal Health

Methionine in Broiler Rations

Experimental results obtained by J. R. Reed, Jr., J. H. Quisenberry and J. R. Couch (*Poultry Sci.* 33:44, 1954) in a series of tests on chicks show that the feeding of methionine at the .05 per cent level produces an increase in growth and an improvement in feed efficiency. Best results are obtained when the amino acid is added to a ration containing fish meal or fish solubles. This would indicate that there is an additive effect of the methionine when the amino acid is fed in the presence of the unidentified factor found in fish products. A significant improvement in growth was not observed when an amino acid was fed in a third experiment although an improvement in feed efficiency did result. From these data it is indicated that the feeding of .025 per cent methionine will produce results that are practically equivalent to those obtained by the feeding of .05 per cent. It is indicated further that the level of .0125 per cent methionine is not sufficient to obtain results that can be obtained by feeding .05 per cent or .025 per cent.

Chymotrypsin in Chronic Animal Infections

The potential value of chymotrypsin in the treatment of chronic infections in animals is indicated in the report of L. E. Johnson and L. C. Ferguson (*Vet. Med.* 49:265, 1954), Chymotrypsin is a highly purified proteolytic enzyme prepared from the mammalian pancreas. It is extremely stable in crystalline form, but rapidly autolyzes in solution at room temperatures. Although it is active in a range from pH 5 to 8, greatest proteolysis is demonstrated about pH 7.1 which can be obtained with a suitable substrate such as Sorensen's solution.

Johnson and Ferguson report on seven cases in which chymotrypsin was used in the treatment of conditions characterized by the presence of purulent exudate and necrotic tissue. It was found that the enzyme digested and reduced to a liquid state all purulent material, blood clots, fibrin formations, and calcifications, and any other dead tissue present in the lesion. Living cells were not affected. There was found to be a transient rise in temperature in some animals which may have been due to rapid absorption of toxic material prior to thorough drainage. No other untoward effects were noted. Experimentation has shown that the dosage of chymotrypsin required to treat adequately any condition is quantitatively related to the extent of the lesion and the amount of material to be digested. Repeat treatments are indicated in widespread involvement where an excessively heavy exudate is present.

Antibiotic Therapy in Animals

G. E. Hawley (*Vet. Med.* 49:300, 1954) points out that although there are at least 41 different antibiotic dosage forms for use in animal medicine, the secret of successful use lies in achieving a sufficient concentration of the drug in at least one of five body fluids. The fluids are: (1) Blood, (2) lymph, (3) cerebro-spinal fluid, (4) urine, and (5) feces.

The routes, with the dosage forms suitable for each are: 1. Per orum. Capsules, pills, tablets, high-level feeds, drinking water medicaments, drenches, boluses, oral sprays, *et cetera.*

2. Per rectum. Capsules, enemas, suppositories, *et cetera.*

3. Inhalants. Puffer dusts, nasal vapors, nasal insufflators for capsule inhalants, volatile oils such as Vicks vatronol.

4. Intranasal. Sprays, puffers, dusts, waxes, greases, salves, *et cetera,* rubbed or smeared on, or in, the nose.

5. Ophthalmic. Eye implants, eye ointments, drops, jellies, washes, *et cetera.*

6. Intravenous. By needle, directly into the vein.

7. Intraperitoneal. By this method the injectable material is placed around the outside of the bowels. The mesentery, or bowel coverings, are capable of absorbing drugs.

8. Intramuscular. By hypodermic syringe, using a long needle thrust into red muscle.

9. Subcutaneously. Just beneath the skin. The material is absorbed quite rapidly.

10. Intrapleural. Between visceral and thoracic pleura.

11. Intrathoracic. Into the thorax.

12. Vaginal. Capsules, douches, sprays, powders, suppositories, *et cetera.*

13. Uterine. Deposited through the cervix into the uterus proper, such materials as douches, sprays, powders, waxes, jellies, *et cetera.*

14. Intracaudal. Into the spinal fluid, by injection between the vertebrae.

15. Topical. Applied directly, such as dusting, spraying or sprinkling an antiseptic on a wound surface.

Aureomycin in Calcium and Phosphorus Requirements in Chicks

Experiments were made by G. S. Lindblad, S. J. Slinger and I. Motzok (*Poultry Sci.* 33:482, 1954) to study the influence of Aureomycin on the calcium and phosphorus requirements of chicks and poults. Aureomycin improved chick and poult weight in all cases. The more inadequate the ration in calcium and phosphorus the greater was the percentage increase in weight due to the antibiotic. Under the conditions of these experiments and on the basis of the calcium and phosphorus levels employed, the antibiotic did not appear to alter the requirement of female chicks but it seemed to increase the requirement of male chicks, for phosphorus.

The calcium and phosphorus requirements of female poults were not appreciably altered by the addition of Aureomycin to the diet. However, a statistically significant interaction was shown between phosphorus and sex, suggesting that male poults have a higher requirement for inorganic phosphorus than the generally recommended levels of 0.4 per

cent. This may be due to the fact that the interaction between antibiotic and sex was highly significant ($P<0.01$) in favor of the male poults.

In general, Aureomycin improved the feed efficiency of chicks and poults. In the presence and absence of Aureomycin in the diet, when the level of calcium was raised above 1.0 and 2.0 per cent for chicks and poults, respectively, the efficiency of feed utilization was decreased.

Swine Helminthiasis

In notable respects, says A. O. Foster (*Vet. Med.* 49:303, 1954) swine helminthiasis is unique and especially challenging. Unlike the situation in any other class of livestock, the losses attributable to parasites of swine are due almost wholly to helminthic species. There are only some 18 species that are of more or less economic importance; every other class of livestock is plagued by more than twice this number.

Because of the hidden effects of helminths, their full economic significance is rarely appreciated. When pigs appear to be doing well, it is too often felt that the presence of a few parasites is of minor concern. This complacency is costly. One adult ascarid may depress the rate of gain by more than 1 pound before pigs reach five months of age. A recent study showed that Strongyloides, the intestinal threadworm, could largely nullify the capacity of pigs to grow, as well as cause morbidity and mortality losses.

The anthelmintic picture in swine is characterized by a paucity of drugs; the seven or so treatments that may reasonably be employed or recommended against worm parasites of this host are notably fewer than those available for use in other classes of animals. Medication is exceptionally efficacious for the control of large roundworms, and the use of an efficient treatment against them is almost always a necessary adjunct to the successful control of swine parasites. The most effective treatment consists in the administration of sodium fluoride (technical grade, tinted) at a concentration of one per cent by weight of dry, ground feed for a period of one day. Sodium fluoride also has good action against stomach worms (Ascarops) and some action on nodular worms. Against the latter, however, phenothiazine is more effective. It is not possible to comment on the comparative merits of sodium fluoride and cadmium oxide as ascaricides, but it is hoped that this situation will be studied shortly. The other anthelmintics that are available for use in swine, namely, carbon disulfide in ascaropsiasis and chenopodium oil, hexylresorcinol and santonin in ascariasis, are poor secondary choices.

It is noted that no medication can be recommended against some 11 of the 18 comparatively important species. Among those that cannot be treated, in addition to species already named, are gullet worms, red stomach worms, and hookworms.

Methylpentene-ol as a Canine Sedative

Methylpentene-ol was used by W. M. W. Taylor (*Vet. Rec.* 66:359, 1954) in canine practice as a sedative in a variety of cases and subjects. His findings indicate that methylpentene-ol is a useful drug for the pacifying of nervous patients. In some cases it may be useful for helping to induce sleep. The probability is that it will prove to be of value in other circumstances, for example, as an adjunct to general anesthesia. It does not appear to be analgesic. Toxicity and danger from large overdose are apparently of small significance, but much more knowledge of the therapeutic dose range is necessary before the drug can be used to best advantage. The drug is given by mouth in the form of soluble capsules. It is quick-acting and rapidly eliminated. It probably retards the metabolic rate and reduces reflex action time in large therapeutic doses.

Furazolidone for Fowl Typhoid

During studies on the chemotherapy of experimental fowl typhoid, H. W. Smith (*Vet. Rec.* 66:215, 1954) found that one substance, furazolidone, was greatly superior to all others so far tested. The great disadvantage of the other agents was that infected chickens, having been treated with them, frequently continued to excrete *Salm. gallinarum* in their feces, and, consequently, were a source of danger to healthy chickens.

Furazolidone is one of the nitrofurans, its formula being N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone. For use it was mixed in a commercial mash to give a final concentration of 0.02 per cent. Of a total of 90 chickens that were treated only two died. Only one of the 88 survivors developed agglutinins to *Salm. gallinarum*, this chicken also being the only one found to be excreting *Salm. gallinarum* in its feces after treatment was discontinued. In contrast 21 of the untreated chickens died, and the nine survivors were positive to the agglutination test and were excreting *Salm. gallinarum* in their feces. No toxic symptoms were noted when mash containing 0.02 or 0.04 per cent furazolidone was fed continuously to day-old and four-week-old chickens for three weeks.

Trace-Mineralized Salts for Pigs

The use of trace-mineralized salt in animal feeding has increased during recent years. Experimental work at several experiment stations has shown that the addition of the trace minerals, manganese, cobalt, iron, copper and iodine, to a ration will often improve growth and feed efficiency in swine. In these experiments trace minerals have been added directly to the mixed ration and have not shown the value of a trace-mineralized salt when included in a mineral mixture fed free choice. Although trace minerals may not always be needed, the simplest manner of adding them to a ration is to self-feed a mineral supplement containing trace-mineralized salt. This was done in the tests made by R. C. Wahlstrom and R. F. Wilson (Circ. 108, South Dakota Agri. Exper. Station, June, 1954) in which 130 weanling pigs were used in two trials to study the effect of replacing common salt with trace-mineralized salt in a simple mineral mixture. The trace minerals present in the salts used in these two trials were manganese, cobalt, copper, iodine, iron and zinc.

Pigs receiving a mineral mixture of equal parts of trace-mineralized salt, steamed bonemeal, and limestone offered free choice gained 0.09 pound per day faster than those which received common salt in the mineral supplement. Very little difference in feed efficiency was obtained in this trial. In a similar trial, but with heavier pigs, in which the salts composed only 20 per cent of the mineral supplements, there was no difference in rate of gain between the two treatments. Approximately one to two pounds of salt were consumed per pig during the period from weaning to market weight. Since the cost of trace-mineralized salt is about one cent per pound more than common salt the added expense is not significant. It is concluded a mixture of equal parts of steamed bonemeal, ground limestone and trace-mineralized salt may be considered a good mineral mixture for self-feeding pigs under South Dakota conditions.

The Suntan Industry

(*Continued from page 462*)

be regarded as being also pigmentogenic. Any immediate pigment formed is obscured or destroyed by the inflammatory process set up by the simultaneous erythemogenic effects. Destruction of pigment takes place only if the irradiation has been carried to an inflammatory stage. Luckeish claims that for the stimulation of equivalent amounts of tan observed ten weeks after irradiation with energy at lines 2967 A. and 3663 A., exposure ratios must be in the proportion of 1:800. This is compatible with the data thus far advanced. Although the exposure requirement is 800 times greater for the longer wave-length, it does not refute the possibility of attaining a direct and immediate tan in sunlight.

Table 4
ENERGY DISTRIBUTION OF SUNLIGHT
(Microwatts per Square Centimeter)

Wave-Length	Noon Sunlight July
2900-3000	0.5
3000-3100	28.0
3100-3200	145.0
3200-3300	312.0
3300-3400	436.0
3400-3600	977.0
3600-3700	557.0

From Luckeish and Taylor[7]

Table 4 sets forth the energy distribution for various wave-lengths of sunlight. Between 2900 and 3000 Angstroms, which of course includes 2967 A., the peak of erythemogenic and pigmentogenic activity, energy density is equivalent to 0.5 microwatts per sq. cm. From 3000 to 3700 Angstroms, the combined energy value is 2455 microwatts per sq. cm. In effect, the situation is this; although for equal pigmentation, 800 times more exposure is required at 3663 A. than at 2967 A., there is present in sunlight 5910 times more pigmentogenic energy between 3000-3700 Angstroms than at 2967 A. The sun is apparently quite rich in direct tanning rays and the potential of immediate tanning emerges as concrete fact, providing the untanned and otherwise defenseless skin can be shielded from the burning rays, 2967 to 3150 Angstroms, which take effect in relatively short exposures. According to Hausser, K. W.,[10] erythemal and tanning activity takes place in the range between 3300 and 4200 Angstroms, with a maximum at 3800 A. and two weaker maxima 3600 and 4080 Angstroms. From this and other parallel experiences, it is safe to attribute pigmentogenic properties to the spectral range between 3700 to at least 4000 Angstroms. If the energy flux in this zone, i.e., 3700 A. to 4000 A., were added to the microwatts accruing between 3000 and 3700 Angstroms, (2955 microwatts), the total increase substantially the feasibility of direct tanning, contingent upon whether or not the skin is spared the inflammatory process set up by the short erythemogenic wave-lengths, which are a constituent of the solar spectrum.

Natural Defence Against Excess Insolation

Pigment or tan, by popular opinion, has been accredited with sole responsibility in the attainment of immunity from solar burns. This is not true. Melanin or pigment is but a secondary defense in the white man, although it is of greater importance in the Negro races. Resistance to ultra-violet burns is acquired by a quadruple phase dermatologic mechanism: Proliferation, or increase in the number of cells; cornification or thickening of the uppermost cells or layer known as the corneum; pigmentation or the deposition of melanin in the basal cells which migrate to the outer layers only when the skin is well tanned; changes in cell proteins. This last function is not too well understood and probably plays a role somewhere in the protective system. Since pigment in the white man is mostly located in the basal cells, which comprise the innermost layer of the epidermis, obviously it can serve here only in a secondary capacity, diminishing the intensity of the longer, non-erythemogenic wave-lengths which have penetrated the stratum corneum, stratum lucidum, stratum granulosum, stratum Malpighii, striking the next layer, stratum germinativum or basal cells.

Protection from Erythemogenic Rays

Skin response to sunlight is governed by the following variable factors; intensity of solar radiation; length of exposure; individual sensitivity. There are a few modifying factors which appreciably alter total actinic effects and which we shall consider in proper sequence. The Luckeish Erythemal data which was set forth in a previous discussion becomes the keystone in the determination of how protection a sunburn preventive should provide. For the sake of convenience Table 1 is herewith repeated.

Table 1
RESPONSE OF AVERAGE UNTANNED SKIN
JUNE SUNLIGHT AT NOON

Minimum Perceptible Erythema	20 minutes
Vivid Erythema	50 minutes
Painful Burn	100 minutes
Blistering Burn	200 minutes

Luckeish defines a Minimum Perceptible Erythema or MPE as being that degree of reddening barely but definitely discernible; a vivid Erythema or VE is a bright red coloration, easily identified and without pain or discomfort; a Painful Burn or PB is characterized by a VE and considerable pain; Blistering Burn or BB, is the fourth stage of ultra-violet reaction and is easily recognized by a high pain level, VE, blistering, peeling and systemic repercussions.

Blondes and red-heads may vary as much as 40 to 170 per cent from average in increased susceptibility to actinic energy. Males are slightly more sensitive than females. As is readily apparent from Table 1, ultra-violet stimulation which will engender a reaction greater than a VE, advances into the burning or injurious stage and will be accompanied by inflammation

(*Continued on page 544*)

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Perfumer's Shelf

Oil of Eucalyptus Eudesmioides Bark

As part of their studies of the chemistry of Western Australian plants, A. Blumann, M. Michael and D. E. White (*J. Chem. Soc.* 1953, p. 788) found that the bark of *Eucalyptus eudesmioides* has a pleasant odor but yields little volatile oil on steam distillation. However, extraction with light petrolatum and ether and steam distillation of the extract gave an essential oil from which were isolated cineole, an uncharacterized hydrocarbon fraction, and borneol and globulol.

Essential Oils of Laurus Nobilis and Mentha Viridis

As part of a study of the essential oils of Sardinian aromatic plants, A. Rattu and A. Maccioni (*Rend. seminar. fac. sci. univ. Cagliari* 22:63, 1952, through *Chem.-Abstr.* 48:7262, 1954) found that the extract from the leaves of *Laurus nobilis* of Capoterra, obtained by steam distillation, was of a yellowish brown color and had an unpleasant odor. It had the following properties:

Specific gravity	0.9278
Specific rotation	−12°53′
Index of refraction	1.4730
Solubility in ethyl alcohol	1:1.09

The following fractions, obtained by distillation, were identified: pinene, eugenol, phellandrene, and cineol.

In another report (p. 69), A. Rattu and M. T. Falqui state that an extract of *Mentha viridis*, obtained by steam distillation was light yellow and turned brown when exposed to air. The taste of the oil was mint-like and burning and it had the following properties:

Specific gravity	0.978
Index of refraction	1.492
Specific rotation	−31,1218
Viscosity	0.5017

The following fractions, obtained by distillation, were identified: linalool, pulegone, carvone and carvacrol. The composition is identical to the Russian or Sicilian mint, but differs from the American and German mint in that the latter do not have carvacrol. The linalool content of the oil is high; amounting to 32 per cent.

Oil of Cyperus Scarosius

It is reported by Y. Naves and Ardizio (*Bull. Soc. Chim. France*, 1954, p. 332 through *Manuf. Chem.* 25:257, 1954) that the essential oil of *Cyperus scarosius*, which grows in India, contains approximately 40 per cent of tricyclic sesquiterpenes, 33 per cent of bicyclic sesquiterpenic ketones and 20 per cent of sesquiterpenic alcohols which are mainly tertiary. The oil is an amber-colored liquid with tenacious odor of cedarwood and also of vetivert, with a marked note of eugenol methyl ether. Its characteristics are as follows:

Specific gravity	0.9679
Refractive index	1.500
Optical rotation	−7.86
Acid number	3.9
Ester number	13.9
Carbonyl value	83.2

The ketones have been identified by their 2,4 - dinitrophenylhydrazones which have melting-points of 204.5°, 205° and 228°, 229° respectively. According to Naves and Ardizio these ketones have not been described before.

Oil of Angelica Sylvestris Roots

According to A. F. Costa and J. C. do Vale (*Perf. & Essent. Oil Rec.* 45:112, 1954), *Angelica sylvestris* is a herbaceous, umbelliferous plant found in wet regions, meadows and the like of Portugal. It is known as wild angelica. Distillation of the roots yielded a yellow colored oil with a pleasant, characteristic odor. The oil had the following properties:

Specific gravity	0.8749
Specific rotation	+68°10′
Index of refraction	1.4746
Acid number	1.6
Ester number	7.7
Ester number, after acetylation	20
Esters	3 per cent
Alcohols	6 " "

Fractionation indicates that *Angelica sylvestris* root oil contains about 80 per cent of a hydrocarbon *d*-limonene. In the most volatile fractions the investigators identified α-pinene and nopinene. It contains traces of furfural.

Turpentines of Pinus Ponderosa

The composition of gum turpentines of Ponderosa pine from four widely separated localities has been analyzed by P. M. Iloff, Jr. and N. T. Mirov (*J. Am. Pharm. Assoc.*, Scient. Ed. 43: 373, 1954). Particularly interesting was the presence of small amounts, ranging from one to two per cent, of methyl chavicol in three varieties of Ponderosa pine, a large percentage of Δ^3-carene and about five per cent of β-myrcene in the turpentine of a variety from northern Idaho.

The crude turpentine from *Pinus ponderosa* from the Black Hills of North Dakota had the following characteristics:

Specific gravity	0.8692
Index of refraction	1.4781
Specific rotation	−2.10

Data obtained by fractionation of the turpentine shows that it contains two per cent *dl*-α-pinene; 38 per cent *l*-β-pinene; 37 per cent Δ^3-carene; three per cent terpinolene; one to two per cent methyl chavicol and 13 per cent *d*-longifolene, and about one per cent unidentified bicyclic sesquiterpenes.

The crude turpentine obtained from *Pinus ponderosa* from Priest River, Idaho had the following properties:

Specific gravity	0.8601
Index of refraction	1.4763
Specific rotation	−2.7°

Fractionation data indicate that the gum turpentine contains about one to two per cent *dl*-α-pinene; 12 per cent *l*-β-pinene; five per cent β-myrcene; 64 per cent *d*-Δ^3-carene; five per cent *l*-limonene; two per cent methyl chavicol; four to five per cent sesquiterpenes, part of which is a cadinene-like sesquiterpene.

TOP NOTES by Fritzsche

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A THOUGHT for th

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which you should spe
you earn."

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September—Aster or
Morning Glory

October—Calendula
or Cosmos

RECOMMENDATION of the Month

AMBRE CONCRETE EXTRA

This month's recommendation is a classical amber specialty of intense sweetness with excellent fixation properties. It gives a perfume composition the same smooth, velvety finish that is produced by the use of natural ambergris. It also blends well with the aldehydes and woody-fruity notes typical of modern perfume compositions. We highly commend AMBRE CONCRETE EXTRA as a valuable component and all-around fixative for extracts, colognes and toilet waters. Priced at $14.00 per lb.; $1.00 for the trial ounce.

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EXCEPT for his fast-moving four years with Uncle Sam—from enlisted Marine private in '42 to Captain in '46—under whose direction he "visited" Saipan, Tinian and Okinawa with final stopovers at Nagasaki and Kyusu, Japan, Rhode Island-born JERRY D'AMICO's residence, rearing and education have been within the New England territory which he has served so commendably as representative of Fritzsche Brothers for the past six years. Prior to this, Jerry had been a practicing pharmacist. He received his registration in pharmacy before his enlistment and in 1943 was awarded his B.S. in absentia by the Massachusetts College of Pharmacy. Based upon this solid background, Jerry's selling approach has just the right blend of dignity with warmth, polish with good humor and technical knowledge with practical understanding. In him, our Boston office has a representative of fine character and personal charm. Asked to give some of his life's highlights, Jerry enumerates these (but not in order of importance): his college years; his service experiences including the harrowing and almost successful sinking of his small attack transport by Japanese suicide pilots off Okinawa; his marriage to his charming and devoted wife, Phyllis, and the births of Karen Ann, Deborah Jane and, just in time to record here, Gerald, Jr., who arrived September 7, 1954; and finally, his good fortune in becoming associated with Fritzsche Brothers, Inc.

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HOUGHT for the Month

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earn."
—T. N. TIEMEYER

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es a perfume com-
roduced by the use
the aldehydes and
compositions. We
a valuable compo-
and toilet waters.

VP BANDWAGON?

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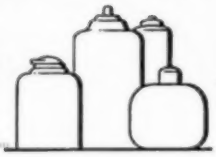
Good Scents
FOR PERFUMERS



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BOUQUET	PVP 837	5.25 lb.
KASMA	PVP 858	7.00 lb.
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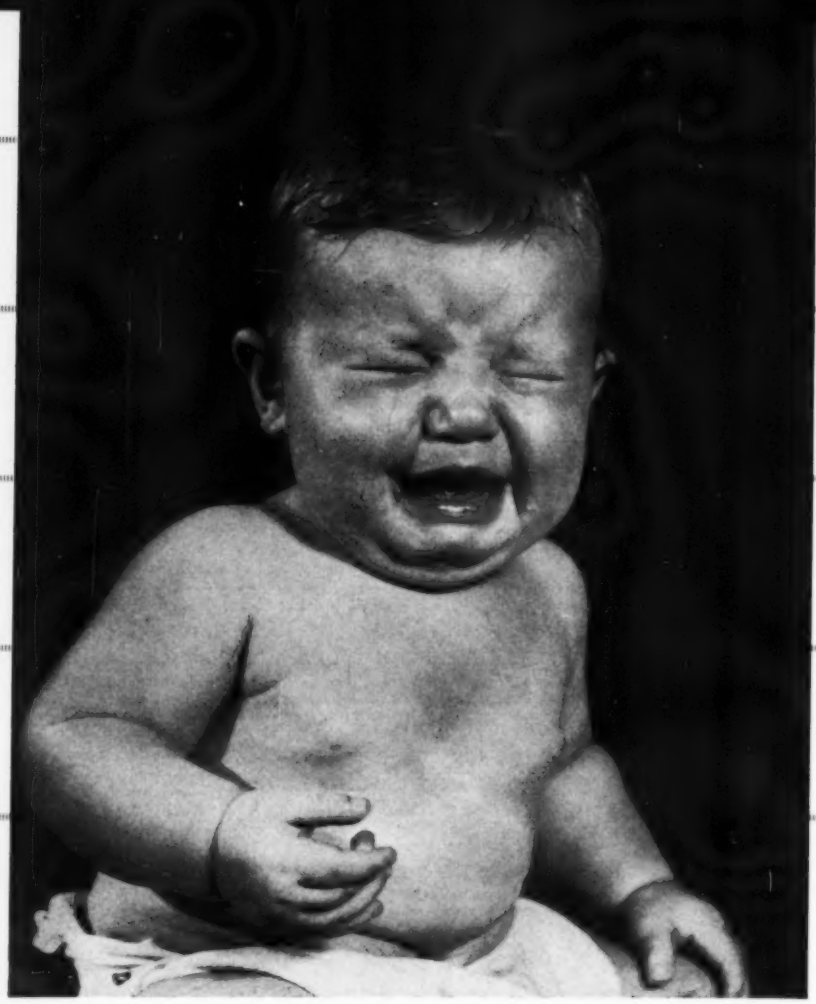

YOU BET I'M UNHAPPY!

"YOU grown-ups just can't seem to understand how bad a nasty old medicine tastes to a little fellow like me! And when you force me to take it, how else can I say I don't like it except to cry?" . . . No doubt baby has a point which all medicine makers should well ponder because the tears and taut nerves and strained tempers that so often result from home episodes like this can be greatly minimized by masking their products' bad tasting ingredients with pleasant and appropriate flavors. Considering all the new knowledge today's flavor specialists have accumulated regarding the applications and compatibilities of medicinal flavorings, there is just no excuse for the pharmaceutical manufacturer's product to be anything but palatably pleasing. If there is room for flavor improvement in *your* products, it's quite possible our flavor experts can help you.

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Iloff, Jr., and Mirov found that the crude gum turpentine from *Pinus ponderosa* from Manitou, Colorado, had the following characteristics:

Specific gravity	**0.8648**
Index of refraction	**1.4761**
Specific rotation	**+1.2°**

Fractionation of a batch of the turpentine indicates that it contains two to three per cent *dl*-α-pinene; 30 per cent *l*-β-pinene; 47 per cent *d*-Δ^3-carene; two to three per cent terpinolene; one per cent methyl chavicol; eight per cent *d*-longifolene and about one per cent *d*-cadinene.

The fourth sample of turpentine, this one obtained from *Pinus ponderosa* from McNary, Arizona, possessed the following physical characteristics:

Specific gravity	**0.8701**
Index of refraction	**1.4730**
Specific rotation	**+13.7°**

This sample was found to contain approximately: 34 per cent *d*- and *dl*-α-pinene; 14 per cent *l*-β-pinene; 31 per cent *d*-Δ^3-carene; four per cent *l*-limonene (suspected but not identified); four per cent *d*-longifolene and four to five per cent unidentified sesquiterpene.

Anti-Oxidants in Spices

According to a note in *Chemical Week* (74:78, June 19, 1954) recent observations by the research committee of the American Spice Trade Association show that two naturally occurring spices, sage and oregano, contain highly effective anti-oxidants. At the Hormel Institute, University of Minnesota, stability tests showed an index of 28 for the sage product, 16 for the oregano antioxidant. Tests were run at 0.02 concentration, at which butylated hydroxyanisole, among the most effective antioxidants currently used in the food industry, had an index of 10. Chemical identification of the spice-derived antioxidants is still pending.

Oil of Artemesia Mogoltavica

M. I. Goryeav, I. M. Shabanov and L. A. Ignatova (*Izvest. Akad. Nauk Kazakh. S.S.R.* 123:75, 1953, through *Chem. Abstr.* 48:6080, 1954) report that the essential oil of *Artemesia mogoltarica* contains 30.77 per cent of carbonyl compounds, including 17.44 per cent camphor, and other substances, including thujone which was identified as the 2,4-dinitrophenyhydrazone, melting at 104 to 106° C. The oil contains 12.3 per cent of cineole, 8.72 per cent of free alcohols, and 10.04 per cent of esterified alcohols.

Storage Effects on Sweet Orange Oil

According to H. T. Islip and W. S. A. Matthews (*Colonial Plant & Animal Prod.* 4:35, 1954) it is generally recognized that for most essential oils the best conditions of storage are in full, sealed containers, in a cool place and protected from light. In the case of citrus oils, good storage is of major importance as these oils are particularly liable to develop off-flavor if stored under unsatisfactory conditions. In their investigations of the effects of storage on sweet orange oil, tests were made on samples expressed from the 1951 and 1952 crops. These studies showed that, after storage for six months in a refrigerator at a temperature of 4° to 5° C. orange oils of the 1951 and 1952 crops had constants which were in good agreement with those of the original oils and it was concluded that little, if any, impairment of quality had taken place. Flavor tests showed that storage at room temperature in the dark affords insufficient protection to prevent some slight deterioration in the quality of the oils. This deterioration was more marked in the case of half-full bottles of oil stored under these conditions. All the oils stored in a north light and a south light at room temperature possessed a decided terebinthine flavor. Fairly rapid deterioration in these samples was confirmed by marked variations in their analytical constants when compared with those obtained for the original oils. The presence of air, as was the case with the oil in half-full bottles, increased the tendency of the oil to deteriorate; where deviations of the analytical constants from those of the original oil were detected these were greater in the half-full bottles than in the corresponding full bottles of oil.

On the basis of these findings, Islip and Matthews conclude that of the three conditions of storage normally recognized as desirable, namely, low temperature, absence of air and absence of light, the most important is temperature. The only difference between the conditions to which the oils stored in the refrigerator and those in the cupboard were exposed was temperature, the former being maintained at a temperature about 15° C. below the latter, yet lowering of quality was apparent under the only slightly less favorable conditions in the cupboard. The indications are, therefore, that if orange oil is to be stored for any length of time, this storage should be at as low a temperature as possible, as well as in the absence of air and in the dark.

Oil of Cultivated Chenopodium Ambrosioides

The essential oil of cultivated *Chenopodium ambrosioides* that was studied by T. Takemoto, N. Takahashi, and T. Nakajima (*J. Pharm. Soc. Japan* 73: 1383, 1953 through *Chem. Abstr.* 48: 3639, 1954) had the following properties:

Specific gravity	**0.9482**
Specific rotation	**—15.33°**
Index of refraction	**1.4875**

Fractionation of the oil yielded 13.9 per cent of *d-alpha*-pinene, 50 per cent of *l*-pinocarvone, 11.6 per cent of ascaridole, and 16.7 per cent of resinous residues.

Oil of Bergamot from French Guinea

R. Schwob (*Industrie parfum.* 8:369, 1953) found that oil of bergamot produced in French Guinea compared favorably with commercial standards for Italian oil of bergamot in olfactory, chemical and physical properties. Commercial scale production was thought to be economically feasible.

The oil was obtained by cold-pressing fruit picked at the "turning" stage. Yields expressed on the basis of the weight of the fruit were 0.73 per cent, an average of five determinations from "Calibrian" trees, and 0.80 per cent, an average of six determinations from "Sicilian" trees. The quality of the oil from the Calibrian trees was superior. Average determinations in 1951 for five Calibrian (A) and six Sicilian (B) samples were:

	A	B
Specificgravity	**0.878**	**0.875**
Index of refraction	**1.4657**	**1.4672**
Specific rotation	**23°47′**	**31°03′**
Acid number	**1.21**	**1.05**
Ester number	**108.9**	**94.6**
Esters, as linalyl acetate	**38.04 per cent**	**34.39 per cent**
Fre alcohol as linalool	**18.22 per cent**	**13.91 per cent**
Fixed residue	**4.49**	**4.11**

Iloff, Jr., and Mirov found that the crude gum turpentine from *Pinus ponderosa* from Manitou, Colorado, had the following characteristics:

Specific gravity	**0.8648**
Index of refraction	**1.4761**
Specific rotation	**+1.2°**

Fractionation of a batch of the turpentine indicates that it contains two to three per cent *dl*-α-pinene; 30 per cent *l*-β-pinene; 47 per cent *d*-Δ^3-carene; two to three per cent terpinolene; one per cent methyl chavicol; eight per cent *d*-longifolene and about one per cent *d*-cadinene.

The fourth sample of turpentine, this one obtained from *Pinus ponderosa* from McNary, Arizona, possessed the following physical characteristics:

Specific gravity	**0.8701**
Index of refraction	**1.4730**
Specific rotation	**+13.7°**

This sample was found to contain approximately: 34 per cent *d*- and *dl*-α-pinene; 14 per cent *l*-β-pinene; 31 per cent *d*-Δ^3-carene; four per cent *l*-limonene (suspected but not identified); four per cent *d*-longifolene and four to five per cent unidentified sesquiterpene.

Anti-Oxidants in Spices

According to a note in *Chemical Week* (74:78, June 19, 1954) recent observations by the research committee of the American Spice Trade Association show that two naturally occurring spices, sage and oregano, contain highly effective anti-oxidants. At the Hormel Institute, University of Minnesota, stability tests showed an index of 28 for the sage product, 16 for the oregano anti-oxidant. Tests were run at 0.02 concentration, at which butylated hydroxyanisole, among the most effective anti-oxidants currently used in the food industry, had an index of 10. Chemical identification of the spice-derived anti-oxidants is still pending.

Oil of Artemesia Mogoltavica

M. I. Goryeav, I. M. Shabanov and L. A. Ignatova (*Izvest. Akad. Nauk Kazakh. S.S.R.* 123:75, 1953, through *Chem. Abstr.* 48:6080, 1954) report that the essential oil of *Artemesia mogoltavica* contains 30.77 per cent of carbonyl compounds, including 17.44 per cent camphor, and other substances, including thujone which was identified as the 2,4-dinitrophenyhydrazone, melting at 104 to 106° C. The oil contains 12.3 per cent of cineole, 8.72 per cent of free alcohols, and 10.04 per cent of esterified alcohols.

Storage Effects on Sweet Orange Oil

According to H. T. Islip and W. S. A. Matthews (*Colonial Plant & Animal Prod.* 4:35, 1954) it is generally recognized that for most essential oils the best conditions of storage are in full, sealed containers, in a cool place and protected from light. In the case of citrus oils, good storage is of major importance as these oils are particularly liable to develop off-flavor if stored under unsatisfactory conditions. In their investigations of the effects of storage on sweet orange oil, tests were made on samples expressed from the 1951 and 1952 crops. These studies showed that, after storage for six months in a refrigerator at a temperature of 4° to 5° C. orange oils of the 1951 and 1952 crops had constants which were in good agreement with those of the original oils and it was concluded that little, if any, impairment of quality had taken place. Flavor tests showed that storage at room temperature in the dark affords insufficient protection to prevent some slight deterioration in the quality of the oils. This deterioration was more marked in the case of half-full bottles of oil stored under these conditions. All the oils stored in a north light and a south light at room temperature possessed a decided terebinthine flavor. Fairly rapid deterioration in these samples was confirmed by marked variations in their analytical constants when compared with those obtained for the original oils. The presence of air, as was the case with the oil in half-full bottles, increased the tendency of the oil to deteriorate; where deviations of the analytical constants from those of the original oil were detected these were greater in the half-full bottles than in the corresponding full bottles of oil.

On the basis of these findings, Islip and Matthews conclude that of the three conditions of storage normally recognized as desirable, namely, low temperature, absence of air and absence of light, the most important is temperature. The only difference between the conditions to which the oils stored in the refrigerator and those in the cupboard were exposed was temperature, the former being maintained at a temperature about 15° C. below the latter, yet lowering of quality was apparent under the only slightly less favorable conditions in the cupboard. The indications are, therefore, that if orange oil is to be stored for any length of time, this storage should be at as low a temperature as possible, as well as in the absence of air and in the dark.

Oil of Cultivated Chenopodium Ambrosioides

The essential oil of cultivated *Chenopodium ambrosioides* that was studied by T. Takemoto, N. Takahashi, and T. Nakajima (*J. Pharm. Soc. Japan* 73: 1383, 1953 through *Chem. Abstr.* 48: 3639, 1954) had the following properties:

Specific gravity	**0.9482**
Specific rotation	**—15.33°**
Index of refraction	**1.4875**

Fractionation of the oil yielded 13.9 per cent of *d-alpha*-pinene, 50 per cent of *l*-pinocarvone, 11.6 per cent of ascaridole, and 16.7 per cent of resinous residues.

Oil of Bergamot from French Guinea

R. Schwob (*Industrie parfum.* 8:369, 1953) found that oil of bergamot produced in French Guinea compared favorably with commercial standards for Italian oil of bergamot in olfactory, chemical and physical properties. Commercial scale production was thought to be economically feasible.

The oil was obtained by cold-pressing fruit picked at the "turning" stage. Yields expressed on the basis of the weight of the fruit were 0.73 per cent, an average of five determinations from "Calibrian" trees, and 0.80 per cent, an average of six determinations from "Sicilian" trees. The quality of the oil from the Calibrian trees was superior. Average determinations in 1951 for five Calibrian (A) and six Sicilian (B) samples were:

	A	B
Specificgravity	**0.878**	**0.875**
Index of refraction	**1.4657**	**1.4672**
Specific rotation	**23°47′**	**31°03′**
Acid number	**1.21**	**1.05**
Ester number	**108.9**	**94.6**
Esters, as linalyl acetate	**38.04 per cent**	**34.39 per cent**
Fre alcohol as linalool	**18.22 per cent**	**13.91 per cent**
Fixed residue	**4.49**	**4.11**

Laboratory Data Sheet

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Type & Name	Usage	Potency (in U.S.P. units per gram)	Additive	Stability	Mesh Size
P1MO Vitamin A palmitate *(liquid)*	In tablets, aqueous dispersions, capsulated products	1,000,000	Edible oil only, for standardization	Excellent	–
P1MO/BHA Vitamin A palmitate *(liquid)*	as above	1,000,000	Edible oil plus antioxidant (butylated hydroxy-anisole). Note 1.	Excellent	–
P1.3 Vitamin A palmitate *(liquid)*	For oil-free preparations	1,350,000 to 1,450,000	None	Excellent	–
A1MO Vitamin A acetate *(liquid)*	In oil solutions and gelatin capsules	1,000,000	Edible oil only, for standardization	Excellent	–
Type P1.8 *(liquid)* Vitamin A palmitate	For research and special production	1,650,000 to 1,800,000	None	Needs special handling	–
Type A2.9 *(crystalline)* Vitamin A acetate		2,800,000 to 2,900,000	None	Needs special handling	–
Type 325 Vitamin A acetate *(dry)*	For tablets, capsules, vitamin-fortified powdered supplements	325,000	None	Excellent	40, 60 and 80
Type 325A-32.5D Vitamin A acetate & Vitamin D_3 *(dry)*		A—325,000 D_3—32,500	None	Excellent	40 and 60
Type 500 *(dry)* Vitamin A acetate	For dry preparations: tablets, capsules, vitamin-fortified powdered supplements	500,000	None	Excellent	40 and 60
Type 500A-50D Vitamin A acetate & Vitamin D_3 *(dry)*		A—500,000 D_3—50,000	None	Excellent	40 and 60
Type 500A-100D Vitamin A acetate & Vitamin D_3 *(dry)*		A—500,000 D_3—100,000	None	Excellent	40 and 60
Type 325A-65D Vitamin A acetate & Vitamin D_3 *(dry)*		A—325,000 D_3—65,000	None	Excellent	40 and 60
Type 250A *(dry)* Vitamin A acetate		250,000	None	Excellent	40 and 60

Note 1 Antioxidant added at 10 mg. per 1,000,000 units of vitamin A.

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Abreast of the Markets

Much Activity in Essential Oils

The essential oil market was buzzing with activity last month, with most houses reporting many price advances and much interest in the various oils on the part of the consumer. Business, they say, is very good.

Citronella Oil Advanced

Formosan citronella oil jumped up to $1.50 a pound toward the end of last month, probably as a result of the Chinese threat to the island of Formosa, combined with the already short supply of the oil on hand.

Caraway Oil Higher

Caraway oil was higher in some quarters during September, with quotations extending up to $4.25 a pound. One factor behind this development is the increased cost in caraway seed.

Peppermint Oil Firming

Although no price change appeared in peppermint oil, this item is becoming extremely firm, and the good quality oil is difficult to find. Demand is steady, and, if it continues, may force a price advance in a very short time. Some houses, in fact, have reported higher quotations on the top-quality oil, ranging up to $6.80 for the natural, and $7.10 for the redistilled material.

Botanicals Plod Along

Although there were a few changes in the botanical field, the activity was limited to a few items. This market continued to be very slow.

Vanilla Beans Extremely Tight

Vanilla beans are difficult to obtain at the present time owing to their scarcity on the spot market. Dealers state that producers in Madagascar and other areas will continue to push the price up because the present demand is far ahead of the supply. While some old crop material is still available, no new-crop beans will appear before the first part of next year.

The Bourbon beans were quoted at $10.50 to $11 during the latter part of September, with the Mexican cuts at $10.25, and the Mexican whole, at $10.50. In many cases, these prices are mostly nominal.

Aloes in Short Supply

Aloes Cape, in previous years a most stable item with few price changes, has become increasingly firm in recent months. The price has advanced sharply, both for the whole material (now 40 cents) and for the powdered which is selling at 48 cents a pound. Dealers attribute the unseasonable weather conditions as well as the disturbed political situation in South Africa as being the chief causes for the advancing aloes prices.

Ipecac Root Reduced

Ipecac root, which has been quite difficult to obtain at reasonable prices for some time, began to decline last month, having been quoted at $7.50 a pound. One of the main reasons for its former high price level was the extensive buying on the part of European interests. However, this buying has decreased considerably in recent months. American dealers cut their purchases to a minimum during the high price period, with the result that an improvement is beginning to be felt in the ipecac market.

Menthol Sluggish

Menthol advanced to $8.50 a pound last month and showed signs of going higher, in spite of the absence of consumer demand. There still has been no great interest in the item, although dealers are looking for a more active market in the immediate months ahead.

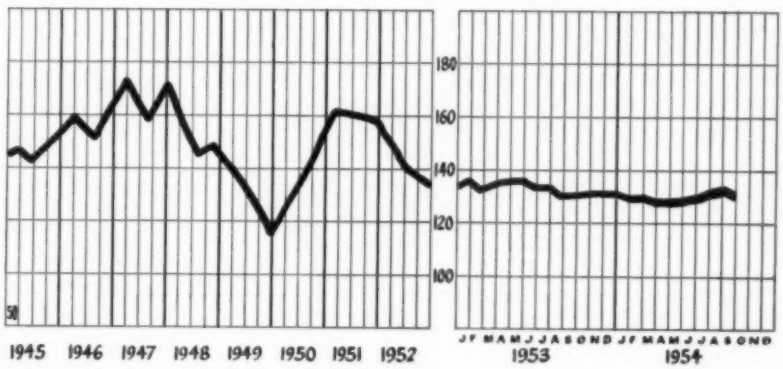
Balsam Tolu Lower

Owing to an improved supply condition in regard to balsam of tolu, the price of the item in some quarters was being quoted as low as $3.75 a pound. The general belief was that the improved price level would remain, and may even decline further. In some cases, the item was selling at the higher figure of $4.25 a pound.

Quince Seed Very Firm

The price of quince seed remained at $2 a pound last month, but this was largely nominal, since there was hardly any material to be found on the spot market. In view of the fact that the new crop has already appeared on the market and no carry-over from last year exists, dealers are looking forward to an extremely firm market for the rest of the year.

50 RAW MATERIALS WEIGHTED PRICE INDEX. 1926 – 100.



The price index of fifty commodities for September declined from 129.5 to 126.6.

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Readers' Questions

Pine Oil Disinfectant: *Our associates are interested in the manufacture of antiseptics in which pine oil would be an ingredient. They would appreciate information regarding formulation. Could you give us any particulars or suggestions as to the source from which it might be obtained without violating any trade secrets?* SAVANNAH. As far as I know, pine oil disinfectant is a standard cleaning and sanitizing aid which is widely used and about which there are not too many trade secrets. Considerable information on such preparations has been published in past years. Pine oil disinfectants are commonly made along the following lines of the Hygienic Laboratory formula:

Pine oil	**1000 parts**
1 wood rosin (acid number-165)	**400 "**
Sodium hydroxide (25 per cent solution)	**200 "**

Heat the pine oil and 1 wood rosin together at a temperature of 80° C. in a jacketed steam kettle, maintain the degree of heat until the rosin is thoroughly dissolved in the pine oil. Drop the temperature to 60° C., add the sodium hydroxide (25 per cent solution) by stirring in very slowly. Saponification should be complete in 30 minutes. This product has a predicted phenol coefficient of 3.5 to 4.

Cream Nail Polish Remover: *Could you favor us with a modern formulation for a cream nail polish remover.* TOKYO. A very stable cream nail polish remover, as offered by Vasic, consists of:

Stearic acid	**9.0 parts**
Castor oil	**2.0 "**
Triethanolamine	**3.5 "**
Butyl acetate	**70.0 "**
Water	**15.5 "**

Melt the emulsifying agent, castor oil and butyl stearate in a jacketed pan and then add the solvent. When all is dissolved, the temperature is raised to 65° C. and then water is added, which has been warmed separately to about the same temperature, and the whole stirred constantly while slowly cooling. Stirring is continued until practically room temperature is attained. Rapid cooling should be avoided and it is particularly necessary to ensure steady stirring through the temperature range 50° to 40° C.

Hair Straightener: *We are interested in the manufacture of a product containing ammonium or sodium thioglycolate, which could be used as a hair straightener for colored people. Any information you can furnish, will be greatly appreciated.* BRAZIL The following formula for a hair straightener has been developed by Keithler and it may be modified to suit your needs:

Polyethylene glycol 6000	2.10	per cent
Cetyl alcohol	13.08	" "
Stearyl alcohol	8.59	" "
Triethanolamine lauryl sulfate	1.09	" "
Propylene glycol	16.28	" "
Water	42.84	" "
Ammonium thioglycolate, 53 per cent	10.45	" "
Ammonium hydroxide, 28 per cent	3.29	" "
Perfume	2.19	" "

Shampoos: *May we request a formula for a milky type lotion shampoo and also a formula for a bland coconut oil shampoo?* MILWAUKEE. A liquid cream shampoo can be made along the following lines:

Sodium lauryl sulfate	85	parts
Polyethylene glycol 400 distearate	5	"
Magnesium stearate	2	"
Distilled water	68	"

A coconut oil shampoo can be made as follows:

Coconut oil	10.00	per cent
Potassium hydroxide, 85 per cent	5.38	" "
Sodium hydroxide, 95 per cent	0.50	" "
Glycerine	12.65	" "
Oleic acid	14.00	" "
Water	56.72	" "
Perfume	0.75	" "

Dissolve the potassium hydroxide in one-third of the water. Melt the coconut oil and add the alkali solution in a thin stream with continuous stirring until saponified. Allow the coconut soap to become cold, stand overnight, before proceeding with the batch. Mix the glycerine with half of the remaining water and bring it to a boil; then add the coconut soap in small portions, and stir until dissolved. Dissolve the sodium hydroxide in the rest of the water and add to the soap solution immediately after the coconut soap has dissolved. Add the oleic acid and stir slowly until completely saponified, then perfume. Age, chill to 32° C. and filter.

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* *The Dispensatory of the United States of America, 1950 Edition*

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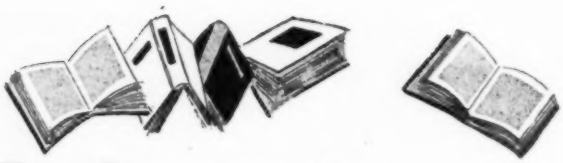

Industry's Books...

Copper, the Science and Technology of the Metal, Its Alloys and Compounds, *prepared under the Editorial Supervision of Allison Butts, Head, Department of Metallurgical Engineering, Lehigh University, with Chapters by Specialists, American Chemical Society Monograph Series No. 122, 936 pp., Book Div. Reinhold Publishing Corp., New York, (1954), Cloth,* **$20.** Almost every phase of the chemistry and metallurgy of copper, its alloys and compounds are covered in this comprehensive book. Forty-six chapters, each written by one or more specialists on the subject, cover all the important fundamental principles, latest practices in the industry, and many of the less well-known applications of copper. Among the many topics receiving such full-chapter treatment are: copper minerals and ore deposits; smelting, converting and refining; melting and casting; hydrometallurgy; physical and chemical properties; corrosion resistance; brass, bronze and other copper alloys; hot and cold working; the physical and analytical chemistry of copper; phase diagrams of binary and ternary copper alloys; details of applications in various industries; copper compounds; and uses of the element in organic chemistry, biology and agronomy. This book will prove useful to all chemists, metalurgists and engineers who refine, manufacture or use copper and copper products.

Physiology and Biochemistry of the Skin, by *Stephen Rothman, M.D., Professor of Dermatology, University of Chicago, 741 pp., Illus., The University of Chicago Press, (1954), Cloth,* **$19.50.** This book is the first to deal with all aspects of the physiological functions and biochemical processes of the skin. Both as a definitive reference work and as a stimulant to further research, it is unique. Discussed in detail are the physical properties of the skin (mechanical characteristics, electrical behavior, and membrane properties in so far as they influence life processes); all pertinent data concerning sweat secretion (the physiology of the glandular function, the composition of the aqueous skin surface film and its hydrogen-ion concentration, the mechanism of insensible water loss through the skin, the role of the skin in thermoregulation, and the phenomenon of prickly heat; the excretion of fatty substances (the physiology of sebaceous gland excretion and the composition of the lipid skin surface film); the

various chemical constituents of the skin (nitrogenous constituents in general, epidermal proteins, including keratins, collagen, elastin, reticulin, connective-tissue ground substance, carbohydrates, lipids, water, electrolytes, pigments, and enzymes). In conformity with its emphasis upon the biological meaning of the data and their variations under different physiologic al and pathological conditions, the book has a special chapter on the physiology, biochemistry, and pathology of the keratinization process and subchapters on a variety of subjects, such as itching in pathological states, anomalies of sweat-gland and sebaceous-gland functions, heat regulation in diseased skin, aberrations of water and salt metabolism, etc. Other special chapters deal with the physiology of cutaneous circulation, the sensory functions of the skin, the biology of epidermal cells, hair growth, nutritional influences, the pathophysiology of blister formation, and the skin's delivery of carbon dioxide to the atmosphere.

Toxic Solvents, *by Ethel Browning, M.D., H. M. Medical Inspector of Factories, 168 pp., Edward Arnold & Co., London, (1953), Cloth,* **$4.** The increasing use of solvents for industrial purposes is liable to cause considerable danger to the operatives who handle them, because there is so little information available on the subject, that the necessary precautions are frequently neglected. The purpose of this book is to remedy this state of affairs, by setting out in convenient form and in simple and straight forward language the properties of those solvents which are injurious to health, and by describing the precautions which should be taken against them. It should prove invaluable to works managers, chemists, engineers, safety officers and similar officials in factories—not only in the chemical industry where solvents are made, but also in the wide range of industries in which solvents are used, and where in many cases their danger is not recognized.

Hypertensive Diseases, Causes and Control, *by Henry A. Schroeder, M.D., F.A.C.P., Associate Professor of Medicine and Director, Hypertension Div., Department of Internal Medicine, Washington University School of Medicine, With Contributions from Gregory S. Gressel, M.D., Dean F. Davies, Ph.D., Mitchell Perry, Jr., M.D., and Donald F. Gibbs, M.B.Ch.B., 610 pp., Illus., Lea & Febiger, Phila., (1953), Cloth,* **$10.** Probably for the first time, hypertension has been specifically controled (not cured) by the sound and accepted medical treatment developed by Dr. Schroeder and his highly qualified co-workers. The therapy is presented in full in this book. Dr. Schroeder has set down all of his vast experience in this field. In doing so, he has clarified the many ideas and experimental findings on hypertension into an orderly concept of etiology and pathogenesis. As a result, the book is highly useful to practitioners who realize today's need for a sound knowledge of the subject. It stresses the basic biochemical and physical influences which are deranged in hypertension, tells how they may be recognized, and when and how to institute proper treatment.

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Louis Kronish, President

(*Continued from page 534*)

and discomfort of some degree—depending upon how far the irradiation is carried beyond the VE point. Therefore a VE response, which is the average reaction of untanned skin to 50 minutes of June sunlight at noon, is the very maximum non-injurious irradiation. Clearly then, protective agents should not permit a photostimulus greater than that which will elicit a VE *regardless* of the time actually spent in the sun.

Sunscreens are available which in certain concentrations can absorb practically all solar erythemogenic energy between 2950 and 3150 Angstroms and simultaneously transmit quite freely the wave-lengths above 3200 A. Such a preparation would enable the user to remain in the sun many hours—long enough to generate a direct and immediate tan without any appreciable erythema. This immediate tan, as has already been pointed out, is attributable to the spectral region above 3200 A. The writer has duplicated this phenomenon in over 25 cases in the Florida sun during April. However such a product would be highly inadvisable except for those pathologically sensitive to actinic radiant energy. The anti-rachitic and probably other physiologic effects of sunshine are ascribed to frequencies between 2950 and 3150 Angstroms. To deprive the sunbather of known and unknown benefits would be a serious disservice to public health. The short or erythemogenic rays are valuable in several other respects. We have already discussed nature's armour against overdosage of photogenic stimulation. Two important phases of this system take place in the corneum or top layer of the skin. These two functions, cornification or thickening of the surface cells and proliferation are set into motion by irritation of cells of the corneum by radiant energy of those wave-lengths absorbed in the corneum. According to Bachem and Reed[11], the corneum absorbs about 73 per cent of incident energy at 3000 A. but absorbs only 30 per cent at 3500 A. and 20 per cent at 4000 A. It is clearly apparent that the corneum had been designed to absorb the shorter wave-lengths. By virtue of such absorption and consequent irritation or injury, a train of reactions are set into motion. Of interest at this point are only cornification and proliferation of surface cells, which we know is the first line of defense against actinic ultra-violet radiation. As is evident from Bachem and Reed, the longer rays are transmitted relatively freely by the corneum. Since energy above 3200 A. is not absorbed, it cannot exert any effect, (energy to be effective must be absorbed), in the corneum. If a sunburn preventive eliminates the erythemogenic band between 2970 and 3150 Angstroms, the corneum will be subjected to any significant stimulation. Without incitement there will be no cornification or proliferation of surface cells and the skin will not have achieved a comprehensive shielding. The skin will still be vulnerable to erythemogenic radiation even though a good tan might be acquired by long wave, non-erythemogenic irradiation, i.e., energy above 3200 A.

Erythemogenic radiation occupies another role in the tanning picture. Luckeish[12] studied the effects of sub-erythemal doses of ultra-violet radiation from an artificial source. Spots receiving intermittent sub-erythemal dosage failed to develop any erythema or tan, whereas areas which were subjected to a single irradiation, 60 per cent less than the combined intermittent exposures, did develop erythema and tan. This phenomenon is of pertinent significance which we shall clarify: From not too conclusive evidence, there seems to be two types of pigment production. According to Blum,[13] short wave radiation which irritates or injures epidermal cells causes the liberation of a melanotactic factor, which in turn stimulates melanization of the epidermis and finally deposition of tan in the basal cells. The longer wave-lengths do not irritate or injure corneal cells and therefore do not initiate the described reactions. These rays which includes the spectral region between 3200 and about 4000 Angstroms are pigmentogenic by virtue of darkening bleached pigment which apparently exists in the skin. It is readily appreciated that a deeper and darker tan can be obtained by the enlistment of both stimuli, i.e., the short and long wave-lengths with their attending different processes.

Henschke and Schulze[9] conducted an interesting experiment wherein water-cooled radiant energy above 3200 A. with the characteristic line spectrum of the mercury arc was allowed to impinge upon skin in which blood circulation had been stopped. No pigmentation followed even though the irradiation was of sufficient intensity to have formed pigment, if circulation were normal. Inasmuch as Blum informs us that non-erythemogenic energy above 3200 A. produces tan by darkening bleached melanin existing in the basal cells, it is the writer's opinion that the absence of blood supply and more directly oxygen, is accountable for the failure to observe pigmentation in the Henschke experiment where the blood supply was cut off. This would seem to indicate that a moderate erythema or synonymously, vasodilation, would facilitate pigmentation. The full biologic significance of erythema is not yet fully understood. Two of the mechanisms relevant to tanning are increased blood supply and some extremely intricate physiologic chemistry. Actually, ultra-violet erythema is a mild injury to epidermal cells, which in turn liberates a number of substances with manifold effects, local and remote. The release of a dilator agent produces vaso-dilation, thereby permitting increased blood supply in the epidermis, which is evident as erythema or reddening of the skin. Another compound, set free only in severe erythema, leucotaxine, is responsible for swelling and edema of the burned and nearby tissue. Proliferation or the building of new and more cells is set into motion and which is an extremely function in the defense strategy. Of paramount consequence in the erythemal train of events is the discharge of what Blum,[13] calls melanotactic factor which is in some manner instrumental in the melanization of the epidermis and the deposition of pigment in the basal cells. However the tan obtained by the short erythemogenic wave-lengths is not as dark, nor as deep

(*Continued on page 546*)

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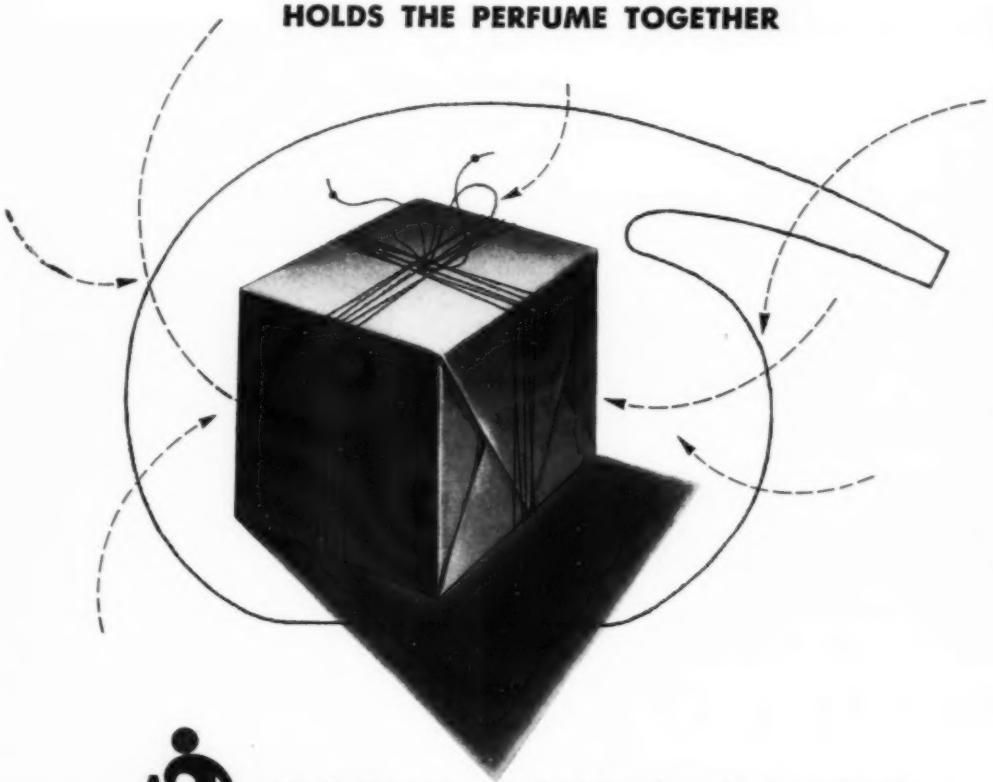

Polak's Frutal Works, Inc., Middletown, New York

*Domestic and Foreign Patents applied for.

(*Continued from page 544*)

or as long lasting as that engendered by the full solar spectrum. The value of moderate erythema to the sun-worshipper is clear. Inasmuch as tanning is so universally and strenuously sought by practically everyone, a sufficiency of erythemogenic radiation to provoke beneficial but not excessive erythema should be permitted. In contradistinction to the advantages of mild epidermal irritation, excess erythematous stimulation or burning will actually retard pigmentation. The author has consistently noted in a study covering thousands of burns, that after a severe sunburn, pigmentation is nominal or non-existent. This phenomenon remains unaltered, i.e., little or no tanning, not only for the balance of that summer but for many succeeding seasons. Obviously one or more of the pigmentogenic factors involved in the synthesis of melanin have been inactivated or destroyed and until recovery or regeneration takes place, there will be slight, if any, pigmentation. To many persons, such deprivation constitutes the loss of a major summer objective. We shall in a later discussion expand this unrecognized syndrome into a powerful selling argument for sunburn preventives.

The actual synthesis of melanin is extremely complex and somewhat controversial. The most accepted theory seems to be the "Dopa" reaction, wherein melanin is synthesized from a precursor, an amino acid, tyrosine, a component of skin. The writer feels, but can offer no proof, that here again oxygen plays a part.

Since tan is so strenuously and universally sought, the sunbather, to take full advantage of the pigmentogenic effects of sunlight, should be allowed a sufficiency of erythemogenic energy to provoke some erythema. This brings us back to our original question, "how much erythema" or how much protection.

Implementation of Erythemal Data

The Luckeish erythemal data acquaint us with the reaction of average untanned skin to June sunlight. We have here two known factors, solar intensity and average dermatologic tolerance. The third necessary unknown is "what is the average exposure?" The writer as early as 1933 concluded that four hours did constitute the average time spent in the sun daily. This was derived from intensive study of public habits on beaches and at pools. Other outdoor activities such as boating, tennis, golf, etc., seem to conform to the same pattern. The factors, average skin tolerance, average exposure and solar intensity, when equated will yield specifications for an efficient and safe sunburn preventive. A 50-minute exposure to June sunlight at noon will elicit from average untanned skin a VE, which is the maximum sub-injurious stimulus. Total time spent in the sun has been agreed upon as being four hours or 240 minutes which is considerably in excess of that necessary to produce a BB. Since it is desired that the sunbather shall not be liable to more than a VE response within this 240-minute irradiation, the protective film or sun-

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burn preventive should not transmit more than 20 per cent of the erythemogenic energy of the solar radiation. Twenty per cent of 240 minutes yields 48 minutes of irradiation computable as 100 per cent effective and this will not provoke more than a VE. Such aninitial dosage means that anti-rachitic, pigmentogenic and physiologic benefits acruing to the erythemogenic wavelengths have been provided without any epidermal discomfort or damage.

Other Relevant Variables

To avoid confusion no mention has been made of certain minor, influential variables which will somewhat alter calculations thus far offered for minimum protective efficiency. The marked declivity in solar ultraviolet intensity before and after meridian is of interest and will entail slight changes in the Luckeish erythemal figures. The Luckeish data is based on peak solar intensity at periods equidistant from noon whereas we are concerned with exposures at hetergenous hours—some equidistant from solar zenith, some intermittent and others hours before or after noon. The writer has postulated that a VE reaction or 50 minutes is the maximum safe irradiation, (48 minutes for arithmetical simplicity). A 48 minute exposure would gain maximum solar intensity, if it would be arranged so that 24 minutes before and 24 minutes after 12 noon constituted the irradiation. This is substantially different than a 48 minute exposure "in effect" spread out over 240 minutes, potentially 120 minutes before and 120 minutes after meridian. Lesser energy flux can be expected at periods such as 240 minutes before or after noon. Another possibility would be two hours in early morning and two hours during late afternoon. In the former situation, where a straight unprotected 48 minute irradiation took place exactly bisected by the solar zenith, maximum solar potency was obtained. In the latter case greatly reduced intensities would be the rule in view of the distances from the noon solar peak. Dorno[15,16,17] investigations seem to indicate an average of about 30 per cent reduction in actinic energy two hours before or after noon. Clark[19] offers information to the effect that with readings of 9000 ergs per sq. cm. at noon in July, there was a declension of 44 per cent at 10:00 a.m. and 33 per cent at 2:00 p.m. Luckeish[20] reveals a parallel reduction. Erythemal intensity at 12:30 p.m. was noted to be 2.4 E-Vitons (E-Viton equals 10 microwatts at 2967 A. per sq. cm.), at 10:00 a.m. and 3:00 p.m. erythemogenic level had descended to 1.5 E-Vitons or 37½ per cent reduction. For the sake of convenience the foregoing declensions were averaged into approximately 29 per cent reduction of ultra-violet intensity at two hours before or after meridian. In view of this phenonenon, changes in the Luckeish Erythemal figures are as follows:

Table 5

Time Required to Produce	At Noon	Two Hours Plus or Minus Noon	Mean Severest Four Hours
Minimum Perceptible Erythema MPE	20 mins.	26 mins.	24 mins.
Vivid Erythema VE	50 mins.	65 mins.	60 mins.

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The small modifications made in Table 5 would not be in order, if an unprotected irradiation were incurred between the hours of 10:00 a.m. and 2:00 p.m., which are probably the hours during which Luckeish made his observations. But our interest lies only in a VE engendered in far less potent hours. Beyond any shadow of question a 50 minute exposure at 10:00 a.m. or 2:00 p.m. will not produce a VE. Energy reception at reduced intensity periods such as just described motivate the changes in Table 5. It is the writer's opinion that a VE response could be attained during a four hour protected irradiation only if 60 minutes of 100 per cent calculable effective energy were allowed to pass. There are periods of the day when even 60 minutes of 100 per cent effective energy reception time will fall short of a VE. For example, an irradiation between 12:00 noon and 4:00 p.m. contains considerably less erythemogenic flux than the hours between 10:00 a.m. and 2:00 p.m. A divided exposure of from 9:00 a.m. to 11:00 a.m. and from 2:00 p.m. to 4:00 p.m. would offer materially less erythemogenic potency than the former exposure. These multiples of irradiations are not theoretical but are actual sunbathing habits. The original transmission figure of 20 per cent permitting the passage of erythemogenic energy equivalent to 48 minutes unprotected irradiation within a total exposure of 240 minutes is now too low. This transmission may be safely increased to 23 per cent which would yield in effect during the quoted average daily exposure, 55 minutes of irradiation to be reckoned as 100 per cent effective and which is still five minutes distant from producing a VE.

Another inconstant of some importance is the remote possibility of a person remaining in a fixed position relative to the sun for as long as four hours. Fatigue and boredom will positively guarantee some body movement and rotation. In this manner all body surfaces would be apportioned exposure time and consequently subdividing appreciably the total irradiation. Potentially, such division between posterior, anterior and intermediate surfaces might be in the ratio of 20:20:10:5 or some other closely related multiple. Therefore it is extremely unlikely that any one surface would be the recipient of more than 75 per cent of the total effective irradiation, or 75 per cent of 55 minutes which yields a net of 41 minutes maximum for any single surface. This is significantly distant from the time necessary to produce a VE, in fact, sufficiently so as to serve as a competent margin to contend a number of other variants that may present themselves. The reflection of short-wave erythemogenic energy from water, sand, snow and ice is formidable. Capacity to cope with augmented intensities under such conditions must be available if a suntan product wishes to offer maximum versatility. Laurens[21] states that the reflection of actinic ultraviolet from water is about $\frac{1}{4}$ that from freshly fallen snow and about twice that from a field of grass. According to Hulburt[22] for the spectral region between 3000 and 4000 Angstroms, reflective powers of tested substances expressed in relative units are as follows: Main sand, 8; Florida sand, 15; Crushed quartz, 40;

Snow, 35; Plaster of paris, 40; White cotton cloth, 36. From the Laurens and Hulburt data, it is abundantly clear that reflection can tremendously augment direct radiation, adding up to a total of erythemogenic potency of dangerous proportions. Serious burns suffered over large bodies of water, especially salt water, are a common experience. Winter sports are fast becoming a substantial market for the suntan industry. Dorno[18] found that in ascending from 1500 to 2500 meters, the increase in ultra-violet of sunlight is greatest below 3200 A., or in the erythemogenic regions. Pettit[23] reports that the total increase in ultra-violet for sky-light and sunlight was five per cent greater at 1737 meters than at 257 meters.This figure is unimpressive by itself but added to the shift towards the burning wave-lengths plus the enormous reflection of actinic rays from snow and ice and the nearly perfect transmission of same through the ultra-clear atmosphere, we have concertedly a multiplication of radiation that is of dangerous intensity. Not only are severe burns easily produced but conjunctivitis or snow blindness are sometimes a dreaded accompaniment.

Another circumstance that will demand the utmost performance of a sunburn preventive is its use in semi-tropical and tropical zones, particularly Florida, the Caribbean and South American resorts. During the winter months, solar intensities in these areas are generally comparable with the northern states during the summer. Throughout the months of April, May, June, July and August, the erythemogenic flux is at least 25 per cent greater in the southern resorts. The excess capacity provided by the 23 per cent transmission factor suggested by the writer, extended by body rotation, will more or less be equal to the extra demands imposed by the environmental conditions outlined. Blondes and red-heads, because of their very definite hyper-sensitivity to ultra-violet energy, must not be neglected. Label text should inform them of their abnormal susceptibility and to compensate for same by either shortening their exposures or the application of several coatings of the protective agent.

A surprising number of persons suffer from the abnormal intolerance to radiant energy of various wave-lengths, mostly in the ultra-violet and visible spectra. Light "allergy" is sometimes used as a blanket term to cover these conditions. The common denominator in all manifestations of photophobia is radiant energy between 2950 and 8000 Angstroms. The clinical pictures of the manifold syndromes are complex and confusing. The basic etiology can be either highly involved or relatively simple, depending upon the disease and whether it occurs on apparently normal or supposed abnormal skin. Whatever the fundamental cause, light is the spark that activates the symptoms characteristic of the particular disease. Treatment by the average practitioner has been anything but satisfactory due to the limited or non-existent understanding of radiant energy and its dermatologic and physiologic effects. However progress is slowly being made. The physician and the patient are learning sun shielding, or

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actinolytic agents can offer prophylactic and frequently therapeutic effects. At the very least, these products in many cases, or even in most cases, can enable heliophobes to enjoy cutaneous contact with the outdoors, without fear of unpleasant or serious repercussions. Any product that is introduced for professional employment, or for use by non-professionals who seek to prevent light dermatoses, must positively be able to fulfill claims made for same. An incompetent product in the hands of a normal person can engender a disabling sunburn and much ill will for the manufacturer. Such a preparation, relied upon by those suffering from pathologic light sensitivity, can be instrumental in devasting injury.

Comprehensive Formulation

No single product can be endowed with protective qualities broad enough to provide wholly satisfactory service in every potential circumstance due to the extreme demands encountered therein. A preparation designed for hyper-sensitive persons or for use in tropical or high altitude areas, would under less severe conditions and requirements, deprive the sunbather of much tolerable and beneficial irradiation. On the other hand an average product created for distribution in the temperate zones for people with normal dermatologic response, would be more or less inadequate for extraordinary situations. The manufacturer who is cognizant of the heterogenous demands to which his preparation might be subjected, and who is not indifferent to same, can pursue one of two alternatives: Furnish detailed directions on how and when to increase protective capacity; market two products, each formulated for the conditions and employment intended. In the former, considerably versatility would be realized by instructing the consumer as follows: "For use in tropics, over large bodies of water or at high altitudes, with or without the presence of snow and ice, more than one application of this lotion should be made." Blondes and red-heads because of abnormal sensitivity to ultra-violet, should also apply several coatings of this lotion." The extra absorption resulting from two or more films of the protective agent, will generally be capable of withstanding unusually powerful radiation, or compensate for pathologic susceptibility. Incidently a double film of a suntan lotion or cream is best attained by allowing one coat to thoroughly dry before applying the second one. The second alternative, marketing two products, is possibly the most advisable expedient with which to capitalize all aspects of the suntan market. One American firm, a pioneer in the suntan industry, which foresaw the widely divergent ultra-violet protective indices that might be indicated, actually does market two separate suntan products. One of these products is reasonably competent for average conditions where exceptional requirements are not demanded. The other possesses an extremely high absorption factor, at least 400 per cent greater than the preparation offered for general use. With protection of such caliber, competency under the most gruelling circumstances is assured. This latter product has enjoyed a tremendous reception by both the public and the medical profession, confirming the wisdom and vision of the manufacturer.

Public Attitude

Our entire discourse on "how much protection" may be concentrated into the claim that for the person of average ultra-violet tolerance and for use under average conditions, a sunburn preventive must not transmit more than 23 per cent of the erythemogenic energy of the solar spectrum. Greater transmission would increase the incidence of excess erythema and burns. Lesser transmission would in some measure deprive the subbather of maximum beneficial irradiation.

The public associates the term, "Suntan Lotion," with protection from or the prevention of painful subburn. Emollient, beautifying and tanning are all fine selling points, and if actually present, are highly desirable virtues. But this one function, the prevention of painful solar dermatitis, must be provided above all else. To those engaged in the suntan industry, this statement should be or become, a basic principle of policy. The public possesses a long memory. A preparation that permits the sufferance of a painful and frequently disabling sunburn, will be remembered for a long time as are all unpleasant things. When the occasion arrives again to purchase a suntan lotion, it is inevitable that he or she will be governed accordingly. An unfortunate aspect of this sort of thing is that the public has been in the habit of condemning the entire industry and of reviving a pernicious hangover of the dim, dead past, "that all suntan lotions are frauds."

One rather successful product emanating from the gold coast of Florida does not make any claims that it can or even is intended to prevent damage from excess ultra-violet irradiation. Rather it is promoted as an aid to tanning. With a clever name and intensive exploitation, an appreciable share of the suntan dollar was captured. The writer conducted no tests and is unable to offer any information relative to its protective ability. Since the manufacturer refrains from making any claims regarding the prevention of sunburn, it is logical but not conclusive, to assume that feeble or no immunity from excess insolation can be expected by its use. As past experience has demonstrated so irrefutably, any product that fails to supply the consumer with this function, the prevention of sunburn, expressed or otherwise, is destined to extinction and the above will be no exception.

Editor's Note:
At a later date, a final installment of this subject covering sun screens and market expansion possibilities will be presented.

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ADEQUATE AND PROPERLY TRAINED PHARMACISTS

(Continued from page 459)

Another productive program provides annual undergraduate scholarships to all accredited colleges of pharmacy. The Foundation allocates up to $400 to each college for scholarships to outstanding junior and senior students who are in actual need of financial assistance to complete their studies. Colleges are required to "match" these Foundation grants, thus stimulating local contributions which double the funds available for undergraduate aid.

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The Foundation appropriates limited support for The American Journal of Pharmaceutical Education, and provides for annual seminars for teachers in pharmacy colleges. These seminars are held in the Summer, and one or more teachers from almost every college of pharmacy are present. With a staff drawn from outstanding teachers and industry workers, these seminars bring the instructors up-to-date in their field. These seminars have contributed to revitalized teaching throughout all our colleges and better training for the pharmacists of tomorrow.

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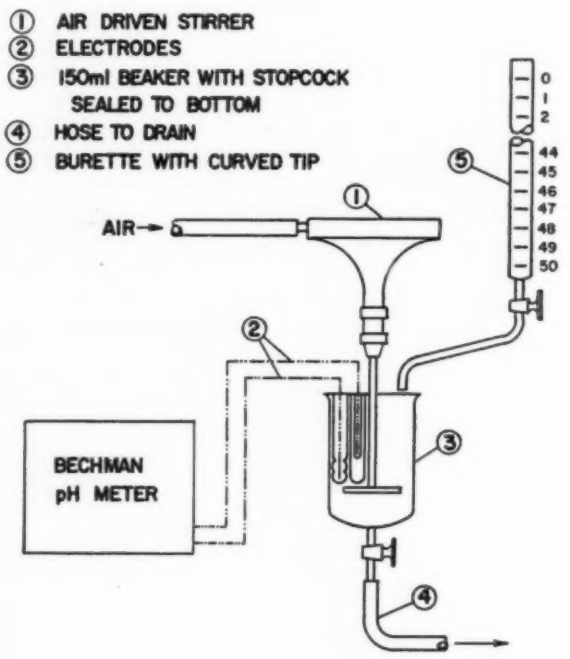
Correction: The following cut was omitted by error from the August issue, page 265 and pertains to the article, Aldehyde Determination by Oximation, by V. D. Johnston.



APPARATUS FOR THE TITRATION OF ALDEHYDES AND KETONES

FIGURE 2 6-8-54

MAKE-UP BASES

(*Continued from page 465*)

after drying of the film the lipophle is strong enough to withstand water damage which might occur due to perspiration. This statement of course covers a large multitude of possible situations but let us say that the better it can perform this function and still retain all its other characteristics the better would be the product.

We have so far discussed cake make-ups which are applied by moist applicators, and the development of a new type in which the water and other constituents are all incorporated in an homogeneous liquid system. There is still another relatively new preparation which merits consideration. This type is a compact face powder from all appearances which is applied as a face powder without simultaneous introduction of water, but which has embodied in it some of the characteristics which serve to produce a matte finish. This new pressed powder is a new form which has incorporated a somewhat higher concentration of covering agency, chiefly titanium dioxide, and also, in most cases, a somewhat small amount of oil to enhance the adhesiveness of the film to the face.

Though this product does not produce as good a smooth finish as does the product previously discussed, it is better than the face powder as such and may therefore be thought of as a cross between the two. It serves in this capacity as an easier package to be carried in a woman's handbag, than does a bottled liquid, and, for this reason, has become increasingly popular. In addition it does not seem to have any of the objectionable functions of face powders insofar as dusting and powdering is concerned. Its popularity as a replacement for face powder has risen to a point where I believe its sales exceed those for the common loose face powder—and this in a relatively short period.

The make-up portion of the cosmetic sales picture is still in a period of great flux. We cannot regard these developments as anything but stopgaps in an otherwise dynamic trend. It would be most interesting to speculate on the form the next stopgap will assume.

PATENT THOUGHTS and TRENDS

(*Continued from page 489*)

velopment of the final wave instead of at or after full development of the final wave in order to preclude further substantial chemical action of the reducing chemical on the curled hair, and maintains the hair in wound form for a period of time sufficient to insure substantial aerial oxidation of the hair for further development of the wave, and after the wave is in permanent fully developed final form, and then unwinds the hair.

The patent naturally claims that generally superior waves are obtained in accordance with the new method. Brown asserts other advantages of his process, one, being the fact that simultaneous waving and styling of the hair can be accomplished using curling rods. Other enumerated advantages are the following:

1. The process represents a virtually foolproof procedure and one which leads to uniformly better waving results.

2. The process is fundamentally more sound than the prior technique because unnecessary chemical treatment is greatly minimized or eliminated.

3. The fixing of the curls is automatic, more thorough, and not subject to error on the part of the individual giving the wave.

4. The physical and chemical properties of the

waved hair closely approach those of unwaved hair.

5. Better lasting waves are obtained due to the more complete fixing of the curls.

6. An improved ringlet curled pattern is obtained, the pattern being manifested even in the heart of the curl.

7. The manual labor required in the given of a wave is greatly reduced.

8. A stronger wave is achieved, yet without the use of harsh waving solutions over prolonged periods.

9. The waving of children's hair is made much less of a problem.

Details showing the operation of the process, as taken from example 1 of the patent follow:

Test tresses of natural hair cut from representative subjects were shampooed, rinsed, towel blotted to remove excess moisture, and treated with a lotion of the following composition:

Ammonium thioglycolate	0.5 N.
Excess ammonium hydroxide	0.5 N. (sufficient to give pH of 9.4).
Wetting agent	0.3 per cent

The tresses, wet with lotion, were wrapped on conventional curling rods using end papers and the wrapped tresses individually re-saturated with lotion. After a 30-minute processing period the tresses were divided into three groups, A, B and C. Tresses A were rinsed with water, unwrapped and allowed to dry; tresses B were sprayed with water and allowed to dry on the rods; tresses C were treated on the rods with a commercial "neutralizer solution" (sodium perborate), unwrapped and allowed to dry.

The tresses were rewetted and tested for strength of curl imparted, the test being repeated in each case after repeated shampooing. The results were as follows:

Tresses	Wet Curl Strength Initially	Wet Curl Strength After 5 Shampoos
A	++	+
B	++++	+++
C	+++	++

It will be observed that the curl in the case of tresses A lost 50 per cent of its strength after five shampoos. The one-third loss in curl strength obtaining in the instance of tresses C is normal with conventional waving lotions. Significantly, the curls formed from tresses B were initially much stronger and relaxed only 25 per cent as a consequence of the five shampoos. Moreover, the curl pattern held up much better.

The properties of the waved hair in the case of tresses B differed little from the properties of the unwaved hair, as shown below:

Tresses	Cystine Content (Per Cent)	20 Per Cent Index
Untreated	17.5	1.00
Waved, rinsed, dried on rod	17.9	0.89

The 20 per cent index is a ratio of the amount of

FOR THE DRUG AND COSMETIC INDUSTRY

ULTRAVIOLET ABSORBERS FOR SUN-TAN PREPARATIONS

hydroquinone diethyl ether
hydroquinone dimethyl ether

PERFUME AROMATICS

hydroquinone dimethyl ether
Compound 77-B

STABILIZERS

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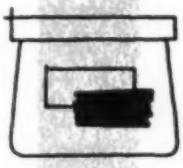

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energy required to stretch an individual hair 20 per cent after the wave compared to that required to stretch the hair the same amount prior to the wave and serves, with the cystine analysis, as a measure of fiber modification.

The point of the Lever Bros. patent, U. S. 2,689,815, appears to be simply to present a more attractive hair-waving composition, the idea being to provide one which has a dense light creamy appearance rather than a translucent, opalescent or watery appearance.

The Lever inventors have found that a finely divided aqueous dispersion of polystryrene and a non-ionic wetting agent, such as a higher alkyl substitution derivative of a moderately high molecular weight polyethylene glycol provides a composition that has the desired opacity and is otherwise an especially advantageous base for hair molding compositions.

The following formulation for a cream hair molding composition is taken from the patent:

	Gm.
Thioglycolic acid	61.0
Sodium hydroxide	27.5
Ammonia	5.8
Lauryl ether of polyethylene glycol (m. w. 900)	10.0
Polystyrene	2.06
Water, distilled	891.5

High Water-and-Salt-Content Milled Soaps

Milled soaps have certain desirable and well-recognized characteristics. Among these characteristics are a uniform texture, firm consistency, a smooth, waxy feel, surface glossiness, grain or crystal orientation substantially in one direction, translucency (when opaque whitening agent is omitted), freedom from warping or distorting as the bars age and dry out, tendency to swell when soaked in water and yet to return to substantially the original shape and appearance after drying, rapid rate of solution in water, especially when rubbed, and consequent profuse lathering power. Other characteristics are the presence of soap in the beta crystal phase, and the lowering of the "thaw point" of the liquid in the bar.

Milled soaps are conventionally made by "milling" a low moisture, low electrolyte soap (e.g. 10-15 per cent water and 0.4-0.6 per cent salt), that is by passing the largely solidified but still plastic soap between a series of rotating rolls, successive members of the series rotating at higher speeds and at closer clearances, the soap being thus subjected to mechanical working, shearing and compacting. The emerging sheets or ribbons of soap are then further mechanically worked, with shearing and compacting, by being forced through one or more orifices of restricted size by the pressure of an Archimedean screw revolving within a closed barrel. The action of the screw in compressing the soap and forcing it through the orifice is known as plodding and extruding. The mechanical working results in a rise in temperature, which may be regulated by adding or abstracting heat as desired. The combined effect of temperature and of extrusion under pressure is to weld the soap together and cause it to emerge from the orifice as a homegeneous, coherent, slightly plastic bar, which is then cut into suitable lengths and stamped for use.

Heretofore, milled soaps have been made only from soaps which are low in water and in electrolyte content. The neat soap of the kettle, i.e. the so-called "kettle soap" obtained according to conventional soap-boiling practice by settling over nigre, contains about 0.4 per cent or more of sodium chloride and up to about 0.1 per cent of sodium hydroxide or Na_2CO_3, but for milling purposes it is excessively high in water, normally running about 30-32 per cent H_2O. Milling of such soap has been unsatisfactory because of the stickiness of the flakes, the softness of the extruded bars and their lack of the desirable milled soap characteristics. A drying process is therefore commonly practiced before milling, whereby the water content is reduced to about 10 per cent to 15 per cent, but this of course adds to the expense of the soap manufacture.

The Procter & Gamble inventors claim that their milled soaps have a high water-and-salt-content.

Example 1 is reproduced below from the patent.

Soap was made by the conventional boiled, settled process from a stock formula of:

23 per cent coconut oil
20.0 per cent marine oil, hydrogenated to 70 iodine value
22.8 per cent tallow, 28.5 per cent lard, 5.7 per cent palm oil — The mixture hydrogenated to 49 iodine value

To the molten kettle soap, which contained 0.4 per cent sodium chloride and about 30 per cent water, there was added in a crutcher enough sodium chloride to bring the salt content to 2.75 per cent. The hot mixture was allowed to cool to room temperature and solidify. It was then forced back and forth 24 times from one chamber into another through a slit orifice $1\frac{1}{2}'' \times 1/32''$ in cross section. The pressure on the high pressure side of the orifice was from 580 to 640 lbs./in.^{2} and that on the low pressure side was 210 lbs./in.^{2}. The chambers, ram, orifice walls and soap were maintained at 110° F. by water-jacketing. The resulting bar of soap formed under pressure in the extrusion chamber was smooth, firm, homogeneous, waxy and translucent. It lathered freely on the hands, was subject to great swelling when soaked in water but returned to substantially its original shape and appearance when dried. Its breaking strength was 29 lbs./in.^{2} when measured by the Mullen tester. X-ray analysis showed it to be in the beta form, whereas a corresponding framed sample was approximately 50 per cent beta and 50 per cent omega. The extruded bar was tested mechanically for rate of wear and lathering power by subjecting it to the mechanical action of a motor driven brush and a stream of water under controlled conditions and determining the amount of soap in the lather formed by this treatment in a fixed length of time. The amount was half again as great as in the

case of another bar of the same soap, containing 2.75 per cent NaCl, which was poured into a frame while molten and allowed to cool slowly to room temperature without agitation; it was 92.5 per cent as great as the amount obtained in a parallel test on a commercially milled, plodded and stamped soap of the same fat formula containing 14 per cent water, 0.38 per cent NaCl, 0.12 per cent Na_2CO_3 and 0.2 sodium silicate.

RECENT PATENTS

2,687,366—**American Home Products—Analgesic containing non-toxic salt of N-methyl-omega-phenyl-tertiary-butyl amine.**

2,687,367—**Eli Lilly—Medicinal Tablet containing Identification Fragments.**

2,687,368—**Commonwealth Eng. — Hydrolysis of Crude Dextran Fermentates.**

2,687,379—**Colgate-Palmolive — Heterocyclic Dithiazine Compounds in Detergents.**

2,687,412,3—**Merck—Preparation of Alkali Metal Penicillinates.**

2,687,416—**Casella (Germany)—Hydantoins.**

2,687,435—**Research Corporation—1, 14-Dimethyl-2-Keto-6, 7-Dihydroxy-2, 3, 4, 5, 6, 7, 8, 12, 13, 14-Decahydrophenanthrene.**

2,687,436—**Merck—Substituted 3 - (2 - Naphthyl) - Cyclohexane. Steroid Ho mones Intermediates.**

2,687,980—**E. W. Blanchard, et al.—Thromboplastin Product.**

2,687,981—**Organon—Steroidal Composition.**

2,688,019—**Burroughs Wellcome — 6 - Aryl - 2, 4-Diamino Pyrimidines.**

2,688,021—**G. D. Searle — Bicycloheptene and Bicyclo-octene-2-Carboxylic Acid Esters.**

EMPLOYEE SUGGESTION SYSTEM IN THE PHARMACEUTICAL INDUSTRY

(Continued from page 463)

Supplies

Three ways exist to get the necessary supplies for the initiation and maintenance of a suggestion system:

(1) Construct your own suggestion boxes and print your own forms, manuals and publicity.

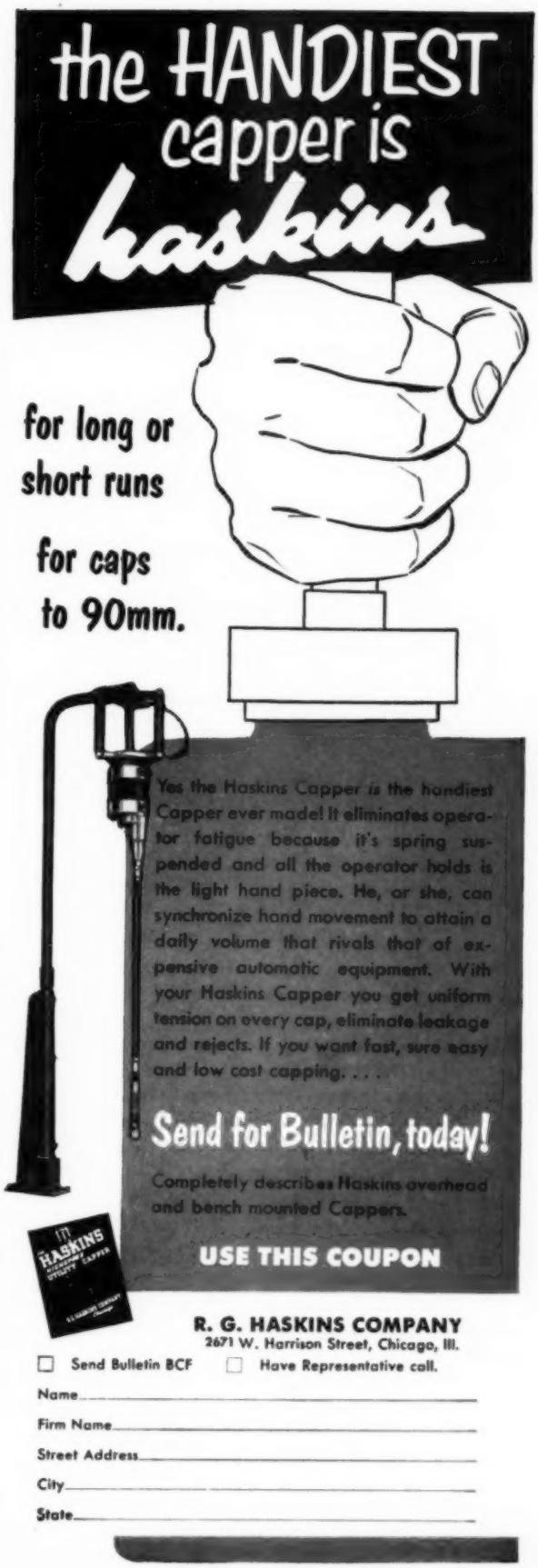
(2) Buy supplies as needed from companies servicing such requirements.

(3) Rent a "packaged" system which provides the necessary supplies.

Many companies use the first technique and rely on their own ingenuity to obtain supplies. Seven of the companies, however, purchase some materials as needed. The survey showed the following:

Five companies use: Elliot Service Company
20 North MacQuesten Parkway
Mt. Vernon, N. Y.

One company uses: Morton Suggestion System
312 West Burlington Avenue
La Grange, Illinois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Only one of the companies participating in the survey uses a complete "packaged" system. The Morton Suggestion System (address above) was the supplier in this instance.

Organization

Most companies have found that administrators are necessary to coordinate the overall functioning of the suggestion system and its committee. The majority reported the use of such administrators (16 have them, two do not) and of suggestion committees (16 have, two do not). The survey showed also that the suggestion system administrator is usually organizationally responsible to the personnel director or similar person (seven companies) or to some member of top management (three companies). Further, eight of the companies use "expeditors" to keep suggestions from being lost in the shuffle. In suggestion system work it is continually stressed that unnecessary delays are very harmful and that "perfunctory administration is deadly blight to the system"[2].

Operation

Although there has been a trend toward situating suggestion boxes in relatively quiet spots to minimize possible participant embarrassment, 16 of the 17 concerns answering this question utilize "busy" locations. It is usually advised that one suggestion box be installed for every 50 to 100 employees; the pharmaceutical industry rated as follows:

1 box per 100 or fewer employees: 8
1 box per 101 to 200 employees: 6
1 box per 201 or more employees: 2

Some sort of suggestion system "bible" for employees and supervisors is essential for smooth operation. Ten pharmaceutical companies reported the use of a special suggestion plan manual for employees, while two have such information in the general employee handbook, and five companies make no provision for the formal dissemination of this information. A commendable trend is the inclusion of most of the pertinent rules and operating details on such suggestion blank. Twelve of the 18 companies reporting also have procedural manuals for supervisory personnel.

The question as to whether supervisors should be eligible for cash awards is a favorite debate topic. There appears to be a growing tendency to permit supervisors to receive cash awards for submitted suggestions which are unrelated to their routine responsibilities. Eleven companies award supervisors for suggestions whose scope is considered "beyond the call of duty." Seven companies, however, do not consider supervisory people eligible for cash awards under any circumstances.

Although suggestion plan veterans do not deem it desirable to put limitations on the types of suggestions submitted, they frequently advise that non-constructive gripes be discouraged. However, in the pharmaceutical industry only seven of the 16 companies responding to this question actually make a point of discouraging such suggestions.

In the past, the policy of most companies was to have suggestions submitted on a strictly anonymous basis. The trend is now reversed as the following survey tabulation demonstrates:

Signature required: 8
Signature optional: 8
Completely anonymous: 1

It might be well to mention that, when included, the suggestor's name is concealed from the suggestion committee and other involved parties by immediately removing it from the suggestion blank and filing it in the suggestion plan office.

The calculation of awards is now pretty well standardized. Generally speaking, awards for accepted tangible suggestions are based on 10 to 25 per cent of the net of the first year savings. Seventeen of the 18 companies also reported a minimum cash award, as follows:

Less than $5.00: 4
$5.00: 11
More than $5.00: 2

On the other hand, 16 companies stated that they have no maximum cash award, although one company has a fixed maximum of $100. The awards in the pharmaceutical industry generally average between $10 and $20, as the survey summary indicates:

Less than $10.00: 0
$10.00 to $19.99: 14
$20.00 to $29.99: 0
$30.00 to $39.99: 1

There is much desirable publicity to be gotten by advertising awards. Items in company papers, house organs and local newspapers provide a very great impetus. It is well to note in connection with awards that cash payments to employees are subject to income tax as earned income. As a result some firms raise the award payment to cover the tax bite and wisely publicize this point also.

It is frequently stated that an effective suggestion system yields approximately 100 suggestions per 100 employees per year. The Pharmaceutical field rates as follows:

50 or fewer suggestions per 100 employees per year: 8
51 to 100 suggestions per 100 employees per year: 3
More than 100 suggestions per 100 employees per year: 3

Perhaps more than any other index, the percentage of suggestions adopted provides an indication of the need and value of a successful suggestion plan. Although nationally it is reported that approximately 25 per cent of submitted suggestions are accepted, the pharmaceutical industry appears to run higher. One company reported an amazing adoption of more than 50 per cent of submitted suggestions. Nine companies reported an adoption of 25 to 50 per cent and two companies stated that they adopt fewer than 25 per cent.

References

Of necessity, the survey and this discussion were only able to deal with the "measurable" high spots of suggestion system work. There are many additional operational details not touched upon here, however, which are vital to successful operation. Because of the importance of thoroughness in creating or improving a suggestion system, the eight following highly recommended publications were culled from the extensive literature on the subject and represent an excellent nucleus of a library.

(1) IDEAS FROM EMPLOYEES, F. A. Denz, Funk and Wagnalls Company: N. Y., 1948.

(2) SUGGESTION SYSTEMS, National Association of Suggestion Systems, 122 South Michigan Avenue, Chicago 3, Illinois, 1944.

(3) GETTING RESULTS FROM SUGGESTION PLANS, H. W. Seinwerth, McGraw-Hill Book Company: N. Y., 1948.

(4) AN EMPLOYEE SUGGESTION SYSTEM FOR A SMALL PLANT, Government Printing Office, Washington 25, D. C., 1952 (15c).

(5) SUGGESTION PLANS FOR EMPLOYEES, Policyholder's Service Bureau, Metropolitan Life Insurance Company, 1 Madison Avenue, New York, N. Y., (free).

(6) SUGGESTION SYSTEMS, National Safety Council, 20 North Wacker Drive, Chicago, Illinois (50c).

(7) MAKING SUGGESTION SYSTEMS WORK, C. R. Riker, American Management Association, 330 West 42nd Street, New York 36, N. Y., 1942, (75c).

(8) GETTING AND USING EMPLOYEES IDEAS American Management Association, 330 West 42nd Street, New York 36, N. Y., (50c).

Acknowledgment

Grateful thanks are due to Mr. Gordon Washburn, administrator of the Suggestion Service of Abbott Laboratories, for permission to use the "Spotlight on Sam" illustration at the beginning of this article. This cartoon is on the cover of Abbott's excellent employee suggestion manual.

Thanks are due also to Mr. H. C. Lundquist, personnel director of White Laboratories, for his kind help with this discussion.

SALICYLATES . . . A MODERN RE-EVALUATION

(Continued from page 457)

ACTH, provided the animal has not been subjected to hypophysectomy or adrenalectomy. This fact demonstrates that the integrity of the functional axis of hypothalamus-anterior pituitary-adrenal cortex is indispensable for this effect.

(2) Administration of Dibenamine does not prevent the salicylates from exerting their effect, indicating that this effect does not consist in the production of a hyper-

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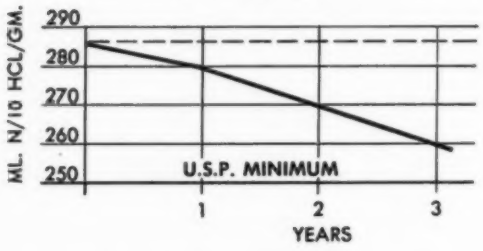

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secretion of adrenalin, a substance that some consider the usual mediator of stress.

(3) The injection of diminishing doses of sodium salicylate reveals the existence of a gradient in the responses of the organism to this drug, the maximum reaction corresponding precisely to a salicylemia of the same degree as that found efficacious in arthritic disease.

Moreover, Roskam and Van Cauwenberge demonstrated in man that:

(1) When the efficacy of the salicylates proves insufficient, one may, with great benefit to the patient, add to the intensive basic salicylate treatment a cautious administration of cortisone (or ACTH) in doses ordinarily considered ineffective.

(2) Symptoms of hypercorticism may appear under the influence of an intensive salicylate therapy or in mixed salicylate-hormone cures.

Many clinical studies have accumulated which point to the similarities in the anti-inflammatory effects of salicylates and the hormones, but the most recent and thorough of these studies is cited here, since it seems to answer most, if not all, of the questions left unanswered in previous work. Under the auspices of the American Conference on Rheumatic Fever, through its Sub-Committee on Criteria and Standards, a study was devised to compare the effects of treatment with cortisone, ACTH, and aspirin on the course of acute rheumatic fever. A report concerning the evaluation of such treatment in young adult males, was published by Houser, et al, in February, 1954.* In 148 young adult males with acute rheumatic fever, 61 of the patients received aspirin; 45 received cortisone and 42 received ACTH. Fever, joint pain and objective evidence of joint involvement were relieved most promptly with aspirin; ACTH was more effective in this respect than cortisone. Apart from the promptness of relief, there was little difference in the three drugs and their effects on the symptoms of acute rheumatic fever. A clinical and/or laboratory relapse or "rebound" occurred in almost all of the patients in each group after cessation of therapy.

Many more studies have added to the basic facts discovered by the above mentioned investigators. Hailman[1], in reviewing the similarities in biologic effects of ACTH, cortisone, and the salicylates listed 16 types of response to ACTH or cortisone administration. In each case an identical response may be obtained with the salicylates.

The accompanying chart lists the criteria adopted by Hailman together with references to papers reporting the responses obtained with ACTH, cortisone and/or salicylates.

It is becoming clear that what was first suggested as a possible theoretical explanation of the anti-inflammatory action of salicylates can now be considered to have the status of a well explored pharmacodynamic mechanism which in itself is a valuable discovery, and which, in turn, may serve to guide experimentalists to further knowledge and further therapeutic understanding.

Our knowledge of these facts should be of the greatest help in putting these drugs to use and in unraveling the mysteries surrounding many other therapeutic agents.

SUMMARY OF SIMILARITIES IN BIOLOGIC EFFECTS OF ACTH AND CORTISONE AND SALICYLATES

1. Causes fall in adrenal ascorbic acid and cholesterol. (3, 6, 9, 10, 11, 12, 13, 14, 15)
2. Causes fall in circulating eosinophiles. (12, 16)
3. Increases 17-keto steroid excretion. (5)
4. Antirheumatic effect. (8, 17, 18)
5. Anti-inflammatory effect. (19, 20)
6. Antipyretic effect. (18, 21, 22)
7. Analgesic effect. (23, 24, 25, 26)
8. Decrease in sedimentation rate. (18, 27, 28, 29)
9. Increase in urinary uric acid excretion. (16, 30, 31, 32)
10. Catabolic effect. (18, 33)
11. Antihyaluronidase effect. (34, 35, 36, 37)
12. Suppression of skin sensitivity reactions. (38, 39, 40, 41)
13. Inhibition of serum vascular disease. (42, 43, 44, 45, 46, 47)
14. Diminishes ocular inflammatory changes. (48)
15. Produces Cushing's syndrome. (4)
16. Protects against anaphylactic shock. (48, 49, 50, 51)

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PROBLEMS IN PRODUCING COMPRESSED AND COATED TABLETS

(Continued from page 467)

powders do not behave in the same manner with respect to the ease with which they can be wetted. Some are particularly resistant while others can be easily wetted. Generally, the finer the particle size the more difficult it is to wet most powders. Particle size, of course, determines surface area and thereby the amount of adsorbed air. Such materials as precipitated sulfur, dried aluminum hydroxide gel and some calcium salts

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are examples of this type of material.

There are several methods which can be used to insure adequate distribution of the granulating solution. The first and simplest is thorough mixing in an efficient mixer. A common fault is the addition of too much granulating solution too rapidly. The criterion universally used to determine when the optimum amount of solution has been added is the "feel" of the mass. Thus when the mixture is thought to have the right consistency, it is removed from the mixer, screened and dried. This "feel," however, can be misleading.

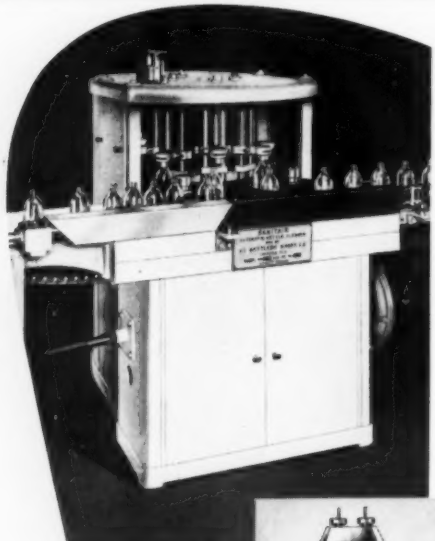
When the granulating solution is added to a mass of powders, the tendency is for the powders to agglomerate into balls using a particularly moist group of powders as the nucleus for the ball. The addition of further granulating solution too rapidly simply coats the surface of these balls and gives the appearance of a wet mass. However, upon close examination it will be discovered that the center of the ball and surface are the only parts in which the powders are sufficiently wetted. To avoid this, the granulating solution must be added in small divided portions, and the mixing allowed to proceed until the powders are uniformly wetted.

The time necessary for adequate mixing will be determined by the efficiency of the mixer employed. In general, a mixer which provides a kneading action is the most efficient. Thus the sigma blade mass mixers are better than the straight blade "pony" type mixers for this application. Passing the damp mass through a hammer mill also aids in the dispersion of the granulating solution. Ideally, a kneader should be used for this stage of the process.

Another means of facilitating the wetting of the powders is the inclusion in the powdered mass of a substance which is soluble in the granulating solution. This is not always feasible, but if an aqueous granulating solution is used, the incorporation of such a material as sucrose in the mass will encourage the spread of the granulating solution.

Another method is the use of a material which will act to enhance the wetting power of the granulating solution. Thus a material such as alcohol which has superior wetting properties can be added to the granulating solution to achieve this effect. However, the incompatibility of most solutions of gums with alcohol makes this a method of limited usefulness. The use of a superior wetting agent such as Aerosol OT in low concentrations in the granulating solution has been found to be extremely effective and is worthy of investigation.

Once the tablet components have been properly wetted, the next step is the drying of the granular mass. In order to facilitate drying, the particles are commonly reduced in size. Usually an oscillating granulator is used for this operation. This machine is simply a device for forcing the mass through a screen of proper mesh size. However current machines of this type are particularly inefficient for this application. The screen usually becomes clogged with the damp mass making passage of further material slow and difficult if not impossible. The fault here lies not with the machine, but



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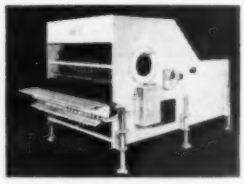

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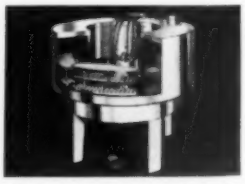

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with the mixing operation. If the granulating solution were uniformly distributed this would not occur. However, because of the general inefficiency of the mixing operation, an excess of granulating solution is commonly added.

The oscillating granulator serves to knead this excess into the powder mass forming a dough which cements the openings of the screen.

In order to sidestep this problem, a hammer mill should be used for the screening of the damp mass. This will not only result in the production of granules, but will also aid in the dispersion of the granulating solution.

The drying of the granulation should take place at a relatively low temperature, usually approximately 50° C. Higher temperatures can result in surface drying and actually retard the escape of moisture from inside the granule by a "case-hardening" effect. Low temperature is particularly important where thermo-labile materials are involved and if a water-soluble color is included, too-rapid drying will cause the color to be drawn to the surface of the mass leaving the lower portions much lighter or even white.

Forced warm air is the most common method for drying tablet granulations although the use of other, more efficient means such as dielectric drying is worthy of serious investigation.

Final screening before lubrication and compression can be carried out using the oscillating granulator. Here again, however, the hammer mill offers a much more efficient operation. The complaint, often voiced, that such milling will result in the production of too many fines is worthy of consideration.

First it must be noted that the speed of milling will influence the amount of fines produced. Thus the mill should be run at low speed with cutting edges forward. It should also be pointed out that in at least one study which investigated the influence of fines it was found that up to 80 per cent of material finer than 80 mesh could be incorporated into a tablet granulation without adverse effect upon the hardness of the resulting tablet. This would seem to indicate that the older concept limiting the amount of permissible fines to 30 per cent is of doubtful validity. While it is true that impalpable powders tend to resist bonding under pressure, it would seem that the hardness of the aggregates, regardless of particle size, is the major determinant of final tablet hardness. Thus the only instances in which the percentage of fines would be critical would be those where the granules themselves are too soft to remain distinct granules under pressure.

In the compression stage the major factor which influences the quality of the tablet is the speed of compression. The force of compression causes the granules to deform plastically and form a cohesive tablet. However, during compression the air between the granules must be forced out. Obviously the more gradual the compression, the more complete will be this ejection of air. Too rapid compression can cause entrapment of air and the resulting tablets will be more easily broken. Unfortunately, current compression machines

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operate within relatively narrow limits with respect to speed of compression. A radical change in the design of such machines is necessary if speed of compression is to be reduced appreciably without reducing the production rate. Perhaps the adaption of hydraulic pressure, which can be slow and steady, will result in a tablet press of wider usefulness than those in current use.

In a modification of the wet granulation process commonly used for the preparation of tablets where the active ingredient is present in a very low concentration and the majority of the tablet is diluent, a blank granulation is employed. In this technique a stock granulation, usually composed of a mixture of sucrose, lactose and starch, is prepared in bulk in advance. When required, the proper quantity of active ingredient is dusted upon these granules, mixed and compressed. This method is popular since it does away with the need for separate granulations for different potencies of the same drug. It is also applicable in cases where it is undesirable, for reasons of stability, to wet the active ingredient with any aqueous material.

The problem that arises in such a method and one which occurs whenever two dissimilar granulations are mixed just prior to compression, is that of the classification of the powders. This classification is the migration of the smaller particles downward in the hopper of the tablet machine, and is caused by the vibration of the machine. If the granulation is entirely homogeneous with respect to the distribution of the active ingredient, this problem is not serious, merely necessitating periodic adjustments to assure uniform tablet weight and hardness.

On the other hand, if the granulations are not homogeneous, as in the instances previously cited, this can cause significant variations in the concentration of active ingredient in the tablets, resulting in too potent tablets at about the halfway mark and substandard tablets near the end of the run.

One method to alleviate this problem is to keep only a small amount of granulation in the hopper and to add more granulation at intervals. Another is to dampen the granulation slightly with alcohol to cause the powder to adhere somewhat to the granules. Both these methods lead to decreased efficiency in operation and the best solution is to discard this method of tablet manufacturing if classification becomes a serious problem.

Slugging or Double Compression

This process offers many basic advantages over the wet granulation method of tablet manufacture. No wetting or drying of the powders is involved and thus the process is considerably shorter. In addition, incompatible substances can be tableted without regard to any problem of instability since water and heat are not involved.

The process involves the production of "slugs" or large tablets which are subsequently screened and recompressed into finished tablets.

There are several drawbacks to this process however. First, the tablets which are generally produced by this method are not as hard as those prepared by wet granulation. Secondly, in order to form satisfactory slugs, a slow, rugged tablet press, capable of exerting tremendous pressure is required. This is expensive in equipment and man hours necessary to continually oversee the operation. In addition, since great pressures are involved, the life of the punches and dies used is relatively short.

A third and most important drawback is the fact that few materials lend themselves to tableting by this method. Only those substances which by their cohesiveness can, in crystalline form, achieve satisfactory bonding under pressure can be tableted by this process and yield a good finished product. Such materials are relatively few.

A recent advance which embodies a modification of this process was developed at Columbia University College of Pharmacy. Briefly, the development resulted from an investigation to discover a material which would have sufficient bonding properties in the dry state to extend the usefulness of the slugging method to a wider range of medicaments. Among all the materials investigated it was found that Carbowax 4000 provided the best answer to the problem. It was possible, through the bonding effect of the Carbowax, to produce tablets of a wide variety of medicinals which were comparable in quality to those made by wet granulation.

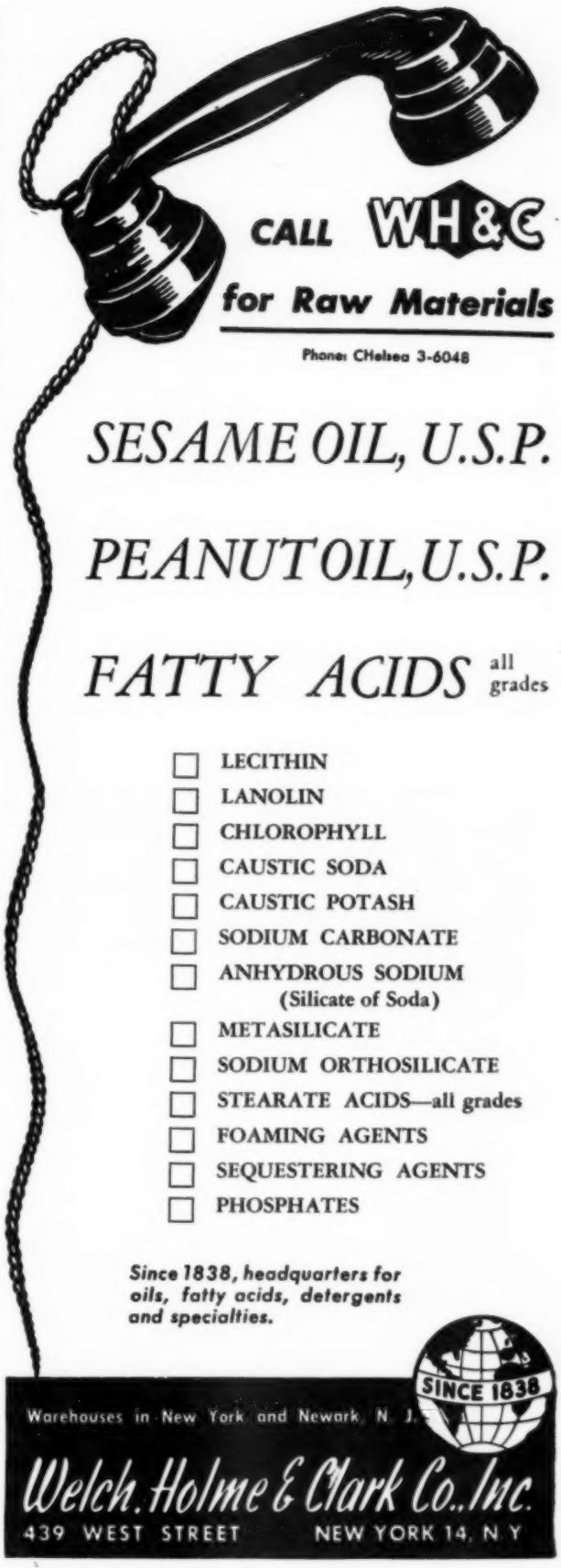
In addition, this process does not require the use of a slow, heavy duty press to prepare the slugs. A single rotary tablet machine is adequate. It was also found that satisfactory tablets of many materials could be made upon single compression. Incompatibilities were noted only with aspirin and sodium salicylate. These materials lowered the melting point of the Carbowax mixture. The problem of classification, discussed above, was completely eliminated.

The general formula which was found to be most widely applicable involved the introduction of up to 20 per cent of Carbowax 4000, 80 mesh, as the binder and the usual amounts of corn starch and calcium stearate as disintegrating agent and lubricant respectively.

The general procedure was simply to mix the finely powdered materials intimately and to compress on a single rotary tablet machine at high speed. The resulting tablets were screened and recompressed if necessary. This procedure thus expands the usefulness of the slugging process with its many advantages while eliminating most of its drawbacks.

Tablet Coating

The coating of tablets involves techniques which have been developed empirically over many years and are used today with little modification of the original. Current tablet coating procedures do not stand as monuments to the science and art of pharmacy but rather are blights upon the name of scientific progress.



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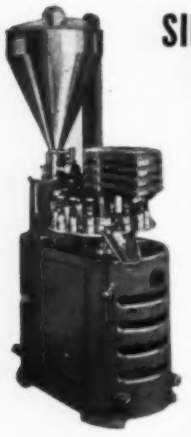

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They involve long and tedious manipulations and days of time for their proper execution and if one batch turns out to resemble a past batch it can usually be chalked up to coincidence.

However, the pharmaceutical industry must be satisfied with these outmoded practices for in the main they seem content to simply indoctrinate new men in the ancient art of tablet coating while they hesitate to devote research facilities to answer the question, why?, with reference to these practices. It admittedly involves less initial expense to continue current practice than it does to modify or change it. Yet in the long run the road of progress in pharmaceutical technology, in order to lead to more efficient and less costly operation, must involve the modification or discarding of outmoded practices.

Tablet coating may be classified into several categories depending upon the purpose of the coating. Sugar coatings are applied to all coated tablets for many reasons which are concerned with the stability, elegance or distinction which the coating confers upon the tablet.

Protective coatings, usually moisture resistant, are applied to increase the stability of labile components, prevent incompatibilities by separating reactive components, or prevent penetration by the aqueous fluids used in sugar coatings. In addition, protective coatings are useful in delaying the release of the medicament from the tablet.

Enteric coatings, which are usually related to protective coatings in so far as composition is concerned, have as their purpose the prevention of tablet disintegration in the stomach, providing release of medicament in the intestine. In actual practice, however, modern enteric coatings are little better than protective coatings, merely delaying the release of the medicament for a sufficient length of time until the tablet reaches the intestine. Generally no enteric coating has consistently met these expectations.

The simple sugar coating requires an average of three days time for its application and is replete with variables to which little heed is paid. Certainly the speed of rotation of the pan, the volume and means of application of the coating solutions, the temperature and humidity of the environment, as well as the size, shape and angle of the coating pan are important variables. Unfortunately little has been done to discover the extent of the importance of these variables.

A modification of the sugar coating process was recently developed at Columbia University College of Pharmacy. It was theorized that the basic difficulty of the process lay in the nature of the material used—sucrose. Sucrose is not a plastic, but a hard crystalline material which powders upon abrasion and tends to make the production of a smooth, uniformly colored coating a difficult and tedious process. It necessitates the application of a subcoat to round off the edges of the tablet since sucrose will not spread and cover the edges. It also requires that the final coats be carefully and slowly applied to prevent roughening.

In the search for a replacement for sucrose among the commonly available plastic materials which could meet all the requirements for a tablet coating material, it was found that a high molecular weight polyethyleneglycol fulfilled the requirements. The coating procedure was developed using a coating solution composed of Carbowax 6000 in Alcohol USP. More recently it was discovered that other high molecular weight polyethyleneglycols could be used.

The coatings applied with these solutions are equal to or superior to sugar coatings as regards quality and smoothness of coat and uniformity of color. They possess the following advantages over sugar coatings:

1. No moisture-resistant protective coatings are required since the vehicle is predominantly alcohol.
2. Subcoating is not required since the material is sufficiently plastic to coat uniformly even standard concave tablets.
3. The time required is considerably shorter than that for sugar coating; one day is sufficient.
4. Coating technique is simpler, easier to learn and reproduce.

Certainly we should be able to develop similar improvements throughout the tablet coating process, particularly in the equipment involved as well as in the techniques of coating.

Protective coatings are becoming increasingly important, especially as more firms are becoming interested in delayed or continual release of medication. Protective coatings on tablets have been used for many years to overcome problems of stability. Certainly shellac dispersions have a long record of usefulness for this application. There are many other materials such as some natural and synthetic high melting point waxes and wax-like materials which are proving even more useful.

The protective coating of granules is perhaps the most interesting recent application of this technique. Such coatings can not only provide gradual and continual release of medicament but can offer a solution to problems of incompatibility and instability in compressed tablet manufacture.

We have recently found that the silicone resins are admirably suited for this latter application. Coating separate granulations of incompatible materials with approximately six per cent of DC Silicone Resin 803 prior to compression was found to be an effective means of reducing incompatibilities in tablets without a great increase in the time required for release of active ingredient.

I would like to conclude with a plea for a more generous attitude by the pharmaceutical manufacturer toward technological research. Certainly the development of superior dosage forms is as important to the manufacturer as the discovery of a new medicinal agent, especially since the effectiveness of the medicinal depends upon its availability from the dosage form and the consumer acceptance of the dosage form.

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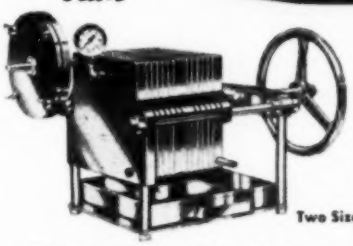

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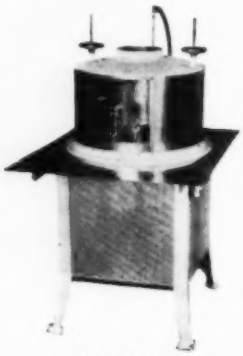

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LYOPHILIZED PHARMACEUTICALS

(Continued from page 469)

centage solids of the frozen plug. However, 0.9 per cent sodium chloride tends to result in a crusty, caked appearance. Lesser percentages of this salt may be used to advantage in increasing plug size. Dextrose has a tendency to carmelize and results in darkened products if subjected to excessive heat during drying. Buffer salts are useful to produce a large volume plug with the fine network of crystals necessary for a solid plug with good reconstitutive characteristics. The mono and dibasic sodium phosphates are ideal in this respect. In non-parenteral lyophilized preparations the percentage of such additives as sodium chloride, dextrose, lactose, sucrose, buffers and stabilizers is not critical; but in parenteral medication, formulation is confined to certain chemical substances and those only to a limited percentage per unit dose of injectable product. With the use of small quantities of inorganic salts it is possible either to raise the bulk volume of the lyophilized residue or to influence the percentage solids of the plug. This is particularly useful in parenteral products.

PROCESSING INCOMPATIBILITIES

It becomes evident that because of the physics of lyophilization, drying by sublimation, that volatile medicinals cannot be included in the lyophilized plug. For this reason, camphor, menthol, eucalyptol, chlorobutanol, benzyl alcohol, ethyl alcohol, choline and other similar medicinals are not found in freeze-dried products. The oil soluble vitamins as A, D, E and K likewise are not lyophilizable due to the oleaginous nature of the vitamin or its ester.

These processing difficulties may be resolved by providing an accompanying diluent containing any of the unlyophilized constituents in a solution which may be used to reconstitute the dried plug to its liquid state immediately prior to use. Additionally, the separation of chemically incompatible medicinals may be accomplished by this dual package arrangement.

FREEZING THE PLUG

A correlation exists between suitable characteristics of the frozen aqueous fill and acceptable lots of lyophilized product. Freezing characteristics such as temperature and rate of solidification have marked influence on the success of the finished product. Many pharmaceuticals, particularly those predisposed to form

long needle-like crystals, if frozen too rapidly and if subjected to improper freezing temperature for the individual product, result in plugs of undesirable properties. Such substances should be slowly frozen with constant examination to insure the desired crystal size in the frozen plug, or they may be quickly frozen and allowed slowly to elevate in temperature until they approach their "fine crystal" temperature. During this temperature elevation, the crystalline network appears to rearrange, for the particle size of the ice grains diminishes. A means of checking for the proper frozen grain size is to examine the product to determine if the frozen plug resembles the color of the finished product. Usually if this condition exists, a suitable lyophilized plug which will remain intact will result.

Departure from the correct granule size in the plug will cause darkened or discolored products, crusts, fissures, heterogeneous plugs, bubbling during the drying cycle, and, in some cases, remelting of the product during sublimation. Van der Held[4] substantiates these views concerning the effect of grain size and its influence on capillarity, thermal conductivity, and heat of vaporization. He concludes that grain size is of prime importance because of its direct relationship to molecular interaction as applied to the boundry layer concept of vaporization.

A desirable temperature range for the frozen plug immediately prior to vacuum drying of many pharmaceuticals is $-30°$ C. to $-35°$ C. The individual temperature peculiar to each product should be determined for best results.

The transfer of product from freezer chest to vacuum chamber may have a detrimental effect on the plug if performed at lower temperatures causing excessive container frosting. This may occur despite temperature and humidity control due to a great temperature differential between container and atmosphere. Subsequently, these frosted containers may cause several undesirable effects when processed. A longer period of vacuum subjection is necessary to reduce the chamber to the 100 micron level because of the rapid vaporization of this shell of ice surrounding the container. This interrupts the quick and regulated introduction of the energy source to aid in the sublimation of the product thus delaying the cycle. In addition the vaporization of this shell may induce self freezing thus further lowering the temperature of the product and in some cases changing the grain size of the frozen plug. Self freezing is induced by the vaporization caused by slowly drawing vacuum from the chamber.

Transfer from freezer to vacuum chamber at too high temperatures often results in melting of the frozen plug, evidencing that such temperatures too closely approach the melting point of the frozen plug.

DRYING CYCLE CONTROL

Of recognized importance is the proper regulation of the drying cycle during lyophilization. The effectiveness of the unit may be impeded by improper operation and inadequate control. Obviously, a short process

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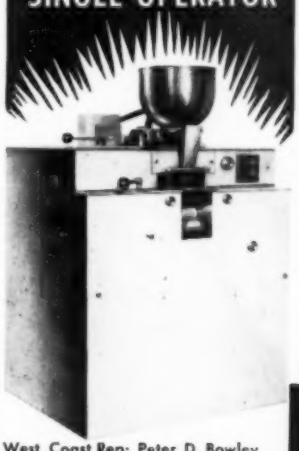

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time with a minimum of loss due to rejected products is desired for profitable production. Adequate control of processing as well as collected data for individual formulae are of stellar importance in achieving lyophilization efficiency.

To insure closer control of the freeze-drying cycles, chambers for freezing and vacuum drying may be equipped with thermocouples which are inserted in the liquid fill and frozen into the plug thus enabling the recording of product temperature throughout processing. A continuous recording device registering product temperatures at various points throughout the chamber may be used to collect data and to provide a permanent record of each production lot. A typical recording would show a continuous series of temperature readings as illustrated in Figure I, Page 469.

END OF DRYING CYCLE

When is the drying process complete? This is the query of essence. Energy cost, equipment wear, production scheduling and product acceptability are all related to this question. The ability to ascertain the completion of the second phase of drying which is the extraction of the last traces of ice crystals is of importance in determining efficient production cycles and in the elimination of costly "melt-backs," lots of material which liquefy when removed from the drying chamber.

The length of the lyophizing cycle is essentially influenced by the amounts of heat supplied to aid in sublimation. It is therefore desirable to apply heat as soon as practicable and to maintain the energy input at its maximum throughout the cycle. Such accelerated drying can only be maintained by accurate control of heat input, high vacuum, and proper adjustment of sublimation and condensation temperatures[3]. The initial phase of vacuum drying by infra-red radiation with its rapid sublimation of ice is easily discernible by microscopic examination via viewports. The product assumes its finished color and texture initially as a small layer at the surface. This layer increases and moves downward until the entire plug has assumed its final appearance. However, the end of the secondary drying phase is not detectable by cursory examination. To break vacuum and perform moisture determinations is costly, time consuming and may result in a melt-back. Conscientious recording of experimental and production lot drying-cycle data proves valuable in determining the completion of drying, and the calculation of energy transfer during drying is essential. Once the true cycle for a product has been established for the operating conditions, such an energy summation may serve as a means of control for ensuing lots.

An immediate processing measurement for moisture can be obtained by the use of a pair of vacuum gauges. One gauge measures dry vacuum while the other additionally indicates the presence of vapor pressure due to moisture in the drying chamber. A large differential in readings indicates residual moisture in the plug, while differences approaching zero indicate product dryness. Such measurements used in conjunction with energy input summations may provide the necessary process controls for drying cycles.

MOISTURE

Several techniques are of assistance in maintaining the moisture-free state of the final product. Residual or reabsorbed water not only hastens product deterioration but also hinders the rapid solubilization derived by lyophilizing. The final moisture content of most pharmaceutical products should never be more than one per cent. One-half per cent residual moisture is an acceptable inner specification for such freeze dried products. There is a rapid loss in rate and completeness of solubility when a moisture content greater than one per cent exists in a lyophilized plug.[16]

To eliminate the reintroduction of moisture when vacuum is broken, purified nitrogen which has been dried by passage through a column of sterile dessicating agent and filtered through sterile bacteriological filters is bled into the evacuated vacuum chamber thus adjusting it to atmospheric pressure prior to unloading. Thereby, containers in the chamber are filled with nitrogen. During the time necessary for this gas to diffuse, secure stoppering may be completed.

Prestoppering by means of fluted rubber closures is of advantage in the ready completion of stoppering. A slight pressure exerted over large numbers of fluted stoppered containers can be used to quickly seat such stoppers. An apparatus is now commercially available which may be used to stopper lyophilized vials using sterile technique either under vacuum or in the presence on an inert gas. It is imperative that aluminum seals are immediately machined over the rubber closures to insure an air-tight and moisture-proof seal. The use of paraffin and silicone impregnated rubber stoppers is of aid in insuring longer moisture-free shelf life for the lyophilized product.

FREEZE DRYING EQUIPMENT

Some observations as to the relative capabilities of radiant energy freeze drying units and conductance type drying chambers may be of interest. In the use of either of these units certain advantages and shortcomings arise which should be considered.

In conductance drying the heat must pass up through the entire plug to assist sublimation. This may result in overheating of the bottom of the container. To avoid this a lower temperature drying cycle must be used thus prolonging the processing. Certain formulations, especially those with low melting points, will bubble and crust when conductance drying is used.

On the other hand, it is possible for the operator to control the temperature of the product more effectively with conductance units. The ability to withdraw heat as well as apply heat at any time during the processing cycle is most desirable for processing. If heat is applied too quickly or if vacuum is insufficient, the product can be maintained in its frozen state or refrozen without breaking vacuum or removing product containers to a freezer chest. This is time and labor saving and aids in

maintaining sterility. Many radiant energy drying units make no allowance for refreezing without removal to separate freezer chest.

Attention should be focused on errors produced by thermocouple readings taken in units utilizing radiant energy heating sources. Zamzow and Marshall[14] noted the result of penetration of energy to the thermocouples imbedded in the frozen plug resulting in temperature recordings higher than the temperature of the product in process.

Of particular interest is a comparison of the energy requirements of both type drying units. Zamzow and Marshall[14] concurred in the observations of Levinson and Oppenheimer[9] tabulating a comparative drying rate for radiant energy of 0.134 lbs./(hr.)(ft.^{2}) with a corresponding value of 0.077 for conductance freeze drying. In addition the terminal phase of the drying cycle in radiant energy drying is diminished with respect to the overall cycle.

Should the product separate from its container during drying, the cycle is greatly prolonged with conductance drying while there is a similar but lesser effect with radiant energy sources. It is imperative that containers used shall not be silicone treated for such surface treated vials will exhibit this break-away of the plug from the container wall. In organic salts added to the formulation as buffers or isotonicity producers tend to produce products which adhere to their containers.

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KEEPING PACE WITH THE ANTIHISTAMINES

(Continued from page 472)

nausea and vomiting of pregnancy. In his study, 60 patients suffering from gastric disturbances in pregnancy were treated with antihistamines and an equal number were given an inert preparation. The results showed that a high proportion (88 per cent) of the patients obtained relief with these agents and only a small proportion (10 per cent) were relieved with the inert

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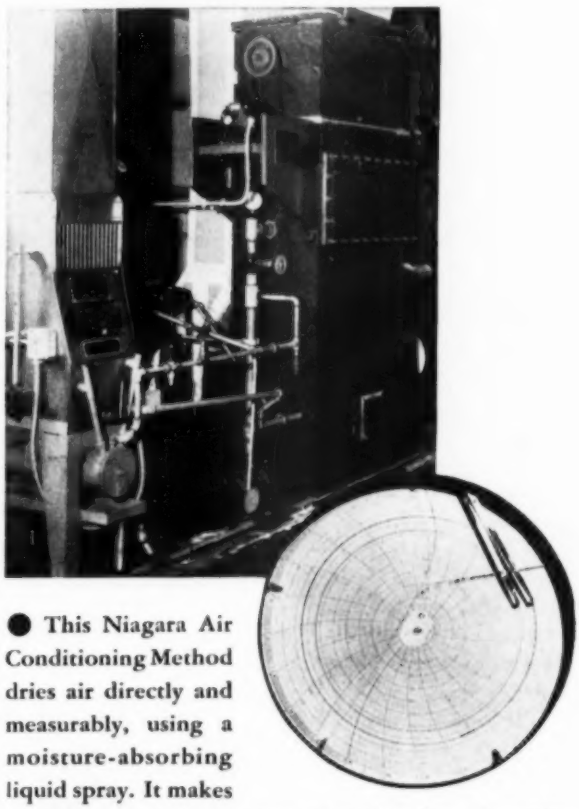

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preparation. Some of the patients who did not respond to treatment, showed improvement after the dosage was increased or a more powerful form of antihistamine was given.

Kaplan and his colleagues[88] have reported that an antihistamine preparation served as an effective adjuvant measure in the treatment of psychogenic vomiting. They cite the case of a young man who had vomiting of two years' duration on a psychogenic basis with a subsequent loss of 30 pounds in body weight. With the administration of the antihistamine there was immediate cessation of emesis and increased appetite. This favorable response to the drug permitted the institution of intensive psychotherapy.

Also highly indicative is the report by Warrington and his associates[89] on the successful use of an antihistamine (diphenhydramine hydrochloride) to control postoperative emesis. The drug was administered intravenously to 106 surgical patients immediately preceding anesthesia. The antihistamine thus given prophylactically protected 87 of these patients from postoperative nausea and vomiting. The antiemetic effect appears to persist for about three hours.

In another group of 58 surgical patients, the antihistamine was not given prophylactically but was administered only in the event of postoperative nausea or vomiting. Fifty-four or 93 per cent of these patients were free of nausea within a few minutes after receiving injections of the drug. Medical patients suffering from severe nausea or vomiting were also treated with the antihistamine. In 18 out of 25 cases in which the drug was effective, the relief lasted for three hours or more. Considering these results, Warrington and associates recommend the routine use of the antihistamine to control postoperative nausea and vomiting.

Other postoperative sequelae have been benefited by the antihistamines. Indicative are the observations made by Kessler and Van Emburgh[90] on 98 cases of surgical trauma and 100 cases of accidental trauma that were treated with antihistamines by the oral and intramuscular route. Their findings indicate that pain is greatly lessened following the administration of these drugs. Edema of accidental trauma, which is of great concern where casts must be applied as well as in other orthopedic problems, was markedly decreased. Similarly, these drugs caused a definite decrease in the edema following surgical trauma, as evidenced by freedom from tissue reaction around the traumatized area and absence of cutting of tension sutures and clips.

Silverman[91] has studied the effect of antihistamines in oral surgery. With these drugs, pain, swelling, bleeding and trismus appeared to be substantially diminished. Local slough was absent and healing occurred more frequently and rapidly. No drains were needed in this group of 555 adult patients, and local treatment was required in only three cases. "Dry sockets" of long standing responded quickly to antihistamine therapy. There were few failures, 21 in the entire series, when the drug was given both precperatively and postoperatively.

The Maslanskys[92] also found that the antihistamines, given parenterally and orally, were valued aids in oral surgery. Postoperative sequelae, such as swelling, pain, trismus and bleeding, were significantly reduced or abolished in patients given an antihistamine as part of treatment.

The oral administration of antihistamines, in addition to local measures, has proved of benefit in the treatment of burns. In a controlled study, Kessler[93] gave such drugs to patients with first and second degree burns. First degree burns responded dramatically to the treatment. Erythema disappeared by the second day and there was no evidence of local edema. In contrast, erythema persisted for three to five days in the control group and approximately 40 per cent developed tissue edema. Patients with second degree burns treated with antihistamines showed less vesiculation and exudation and faster healing than the control group.

In England, Milne and his colleagues[94] administered an antihistamine to all their patients with burns and scalds during a six-months period. The results of this routine measure, they reported, were "striking." In every case so treated the pain was relieved or banished within a few hours, no blistering occurred, and no sepsis developed. The burned areas merely became red and returned to normal within a week. It is important, say these workers, that the first antihistamine tablet be given not later than four hours after the injury.

However, in cases where blistering had already occurred before antihistamine treatment was begun, administration of the drug caused partial or complete relief of pain. In addition the serous discharge dried up within 24 hours and the area became dry and healed in a much shorter time than usual.

In the field of ophthalmology, it has been found that allergic diseases of the eye often respond well to either the oral or local use of antihistamines. Feinberg[1] observes that if allergic conjunctivitis caused by inhalant allergens and associated with rhinitis does not respond satisfactorily to oral medication, the local use of antihistamine eye drops or ointment will often give the desired effect.

In addition to their use in eye conditions which may be allergic in origin, antihistamines may also be administered where atropine-like mydriatic effects are desired. It is said[3] that corneal damage due to various causes may be avoided or diminished by the use of topical antihistamines. In dendritic ulcer, Halleit[95] advises the use of antihistamine eye drops. In cases of extra ocular surgery, such as postoperative pterygia, the use of topical antihistamines hastens the disappearance of vascularization.[96]

In addition to their role as local anesthetics to facilitate diagnostic urethral manipulation, urologists have found that the antihistamines may be useful in the treatment of various conditions of the urinary tract. Herbst,[97] for example, used antihistamines plus chemotherapy to successfully treat nine patients with acute inflammatory lesions involving the urethra, bladder and upper urinary tract.

However, the value of antihistamine treatment of acute nephritis has been questioned. Earlier findings which suggested that these agents might be of value in this disorder were not confirmed in Lawson's[98] more extensive studies.

Apparently results are more consistent when antihistamines are used in the treatment of dysmenorrhea. Macpherson[99] achieved excellent results in the treatment of this painful menstrual condition with the oral administration of various antihistamines. Relief was prompt, generally within 24 hours, in the successful cases. Similar striking benefits was reported by Orban[100] who prescribed an oral antihistamine for a group of 38 patients with essential dysmenorrhea. All of these women were completely or largely relieved of their symptoms.

All 20 of the cases of primary dysmenorrhea treated by Maietta[101] were relieved by the administration of an antihistamine (thephorin). In his opinion, such antihistamine therapy for the symptomatic relief of primary dysmenorrhea appears to be safe, practical, convenient, and economical. It gives prompt and effective relief, can be given orally, is attended by minimal and inconsequential side effects, improves morale, and allows a continuance of normal activities.

Many drugs have been tried in the treatment of Parkinson's disease (paralysis agitans) and trials with the antihistamines indicate that these agents may be of benefit in some cases. Illustrative are the results obtained by Cohen and Criep[102] with antihistamines in 17 patients with this disease. In 12 cases there was slight to moderate improvement of some symptoms, but five patients failed to show any response. Relief of symptom occurred only in the cases classified in the early and moderately advanced stage of the disease.

The symptom responding most favorably was tremor of the extremities, especially of the hands. Associated with this response was a decrease of muscular hypertonicity and rigidity, with, to a less degree, a gain in voluntary motor power of the extremities and diminution in salivation. When a beneficial effect occurred it was observed in five days to a week after the beginning of treatment. Therapeutic response was present only so long as the drug was administered.

It is probable that better results in this disease can be obtained by combinations of an antihistamine with one of the solanaceous drugs. Several investigators[103-104] feel that such combinations are superior to the individual components used separately.

The antihistamines have been tried in the treatment of other nervous conditions with varying degrees of success. For example, O'Leary and Gitt[105] suggest that antihistaminic drugs may be useful adjuncts in the therapy of vertigo. Recently, Vaisberg[106] reported amazingly consistent and rapid gratifying results in the treatment of migraine with injections of dimenhydrinate (Dramamine). In each case, says he, there was complete subsidence not only of the nausea but total relief of the pain within four minutes when the drug was given intravenously, and within 15 minutes when given

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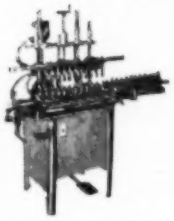

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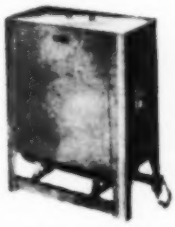

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intramuscularly. He recommends the use of this antihistamine drug for the effective relief of migraine.

In Europe, working on the assumption that a symptomatic psychosis might be the result of an allergic encephalopathy, Tolsma[107] administered an antihistamine to three patients with this condition. Results were favorable.

Martensen-Larsen[108] found an antihistamine to be a useful adjunct to disulfiram (Antabuse) in the treatment of alcoholics. Disulfuram could be given in reduced dosage to intoxicated patients when combined with an antihistamine and sodium chloride. This combination, he reported, prevents nausea and vomiting while providing sufficient sedation. Furthermore, the symptoms of hangover and the craving for alcohol are considerably reduced, if not abolished, during the period immediately following.

A note by Ingram[109] mentions the use of antihistamines in the treatment of two women with Weber-Christian disease, a disorder marked by the formation of painful nodules in the subcutaneous fatty tissue. The lesions cleared in one patient after several day's treatment with an antihistamine and had not returned after three years. The second patient derived some slight improvement from these drugs, but clearance did not take place until cortisone was given.

In Germany, Priessnitz[110] found that patients with olecranon bursitis and painful heels obtained good relief of pain when given intravenous injections of a preparation containing calcium and an antihistamine. He had tried this product after reading of the good results obtained in epicondylitis treated with combined intravenous injections of calcium and the antihistamine, antazoline.

A promising use for antihistamines appears to be in the treatment of pinworms (oxguriasis) which is considered to be one of today's most important pediatric problems. In a clinical evaluation of various agents used to treat this condition, Killingsworth and his associates[111] tried an antihistamine and obtained a high proportion of cures. One investigator in this group, on the basis of 80 per cent cures in 250 cases, believes that the use of such an agent (stripelennamine hydrochloride) is the treatment of choice. It is felt that more studies with the antihistamines in pinworm infestation should be made.

Also pointing to new uses for certain of the antihistamines are studies which suggest that these agents may be suitable replacements for quinidine in the therapy of auricular fibrillation. In their experimental work, McCawley and his colleagues[112] had found that the benzhydryl ether antihistamines prevent ventricular arrhythmias in animals. In tests to determine their value in clinical auricular fibrillation, these workers observed that the antihistamines under investigation prolonged the refractory period at concentrations lower than those required by quinidine. This and other findings led to the belief that the antihistamine, diphenhydramine, was worthy of trial in patients with auricular fibrillation.

In tests[113] on 12 patients with this cardiac condition, six conversions to normal sinus rhythm were obtained with this antihistamine alone when given intravenously. These cases could be maintained by oral administration. In two cases that failed to respond, quinidine sulfate was effective, while the remaining four did not respond to either drug.

Quite recently, Hoffman and his associates[114] made an evaluation of antihistamine therapy in epidemic hemorrhagic fever, a disease that has occurred among United Nations troops stationed in Korea. This type of treatment was tried on the theory that histamine may play a major part in the pathogenisis of the disease. Although the data were difficult to evaluate, there appeared to be a more rapid disappearance of symptoms and physical signs among patients given an antihistamine. While the results were equivocal, it was felt that they suggest the need for further evaluation of the antihistamine approach to treatment.

It is evident from the foregoing indicative rather than comprehensive review that the antihistamines are indeed a versatile group of drugs. The potentialities of these compounds are constantly being explored and sometimes new, often valuable uses are found for them. The indications are that this exploration and evaluation will continue with benefit to the physician and his patients.

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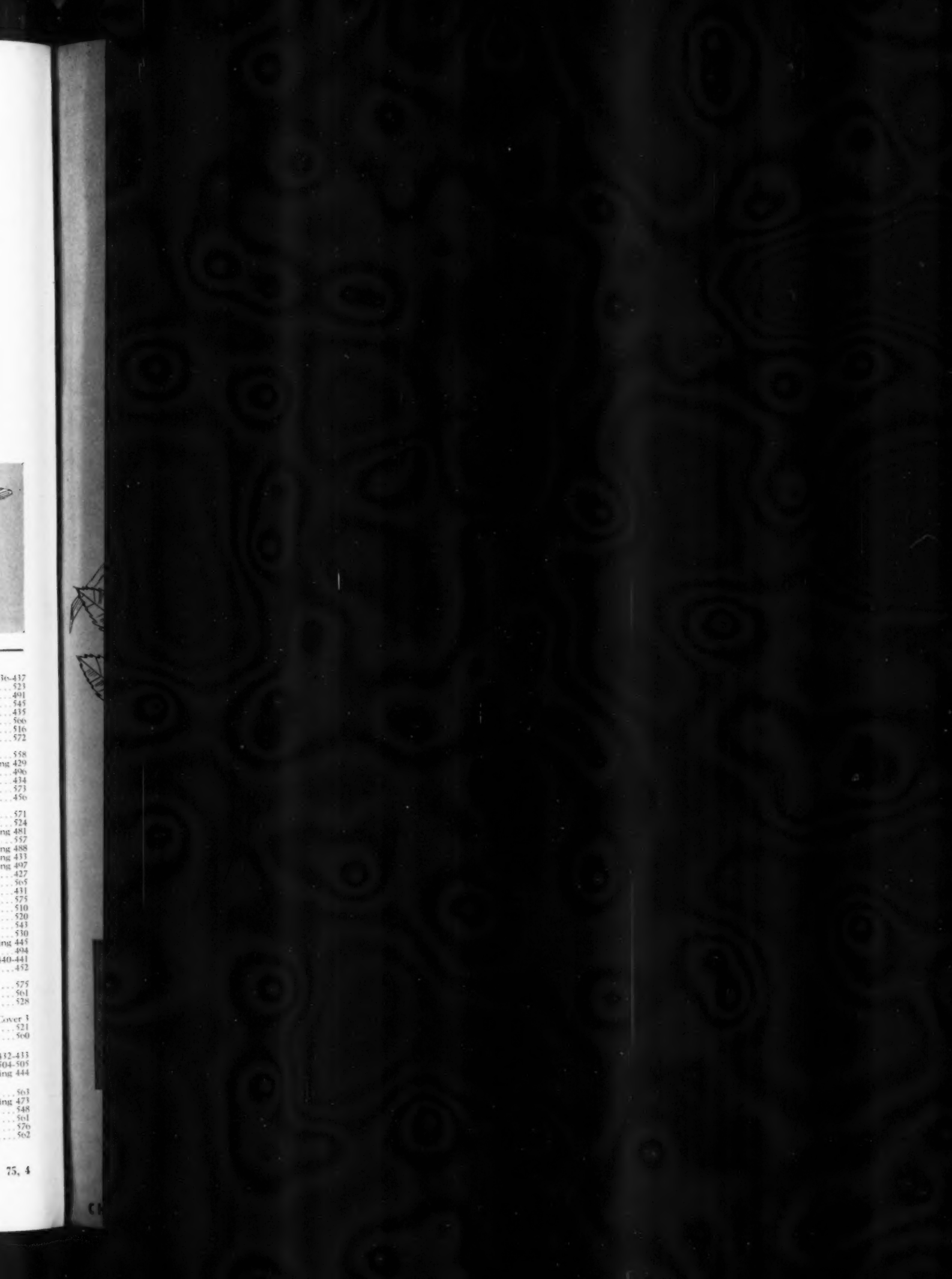

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